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A COMPARISON OF THE RATE OF HYDROGEN EXCHANGE WITH PROTOPHILIC SOLVENTS

A. L. Shatenshtein and E. A. Iakovleva

The work of our laboratory has shown that parallel investigations of hydrogen exchange reactions with acid and basic solvents allow us to draw very full conclusions as to the reactivity of organic substances and also permit an explanation of the rules of hydrogen exchange [1]. For an explanation of the mechanism of the exchange, it is interesting to carry out a reaction of deuterium exchange of dissolved substances with solvents of the same chemical nature, but which differ in their protolytic activity and physical constants. Among the latter, the dielectric constants (DC) of the solvents and dipole moments (DM) of their molecules have particular value. The polarity of the molecules is shown by the reaction between the dissolved substances and the solvents, and the value of the dielectric constant of the latter affects the state of protolytic equilibrium in the solution on which, in turn, depends the rate of hydrogen exchange.

Our work presents a comparison of the rate of hydrogen exchange of a series of substances with liquid ammonia and other protophilic solvents: anhydrous hydrazine, ethylenediamine, and ethanol amine.

TABLE 1

Physical Constants of the Solvents

	Temp.			K_{H_2O}	Ionic conductivity	DC 25°	DM $\mu \cdot 10^{18}$
	melting	boiling	critical				
NH_3	−77.7°	−33.35°	132°	$2 \cdot 10^{-5}$	10^{-33}	16	1.46
NH_2NH_2	2	113.5	158	$3 \cdot 10^{-6}$	10^{-25}	52	1.84
$NH_2CH_2CH_2NH_2$	11	116.2	—	$1 \cdot 10^{-4}$	—	14	1.94
$NH_2CH_2CH_2OH$	10.5	172.2	—	$3 \cdot 10^{-5}$	10^{-6}	38	2.27
H_2O	0	100.0	374	—	10^{-14}	80	1.84

Table 1 gives some constants for NH_3, N_2H_4, $NH_2CH_2CH_2NH_2$, $NH_2CH_2CH_2OH$ (for comparison we give the corresponding values for H_2O). The ionization constants in water solution (K_{H_2O}) give some idea of the relative basicity of the substances but they may be wrong with reference to the anhydrous solvents.

Obtaining Anhydrous Deuterium Solvents*

Anhydrous hydrazine was obtained by the method of Brown and Welsh [2] by ammonolysis of hydrazine sulfate by liquid ammonia for which we used the somewhat modified extractor of V. A. Pleskov [3] (Fig. 1). The siphon which we connected to the receiving flask permitted us to draw off the anhydrous hydrazine into a glass ampoule attached by Wood metal to a steel connection. The latter was screwed onto a metallic apparatus supplied with a valve [4] for the addition of liquid deuteroammonia obtained as described in [5]. The exchange

*In this work substances are called deuterium substituted when they have different deuterium contents; the formulas for the deuterium compounds have a conditional character.

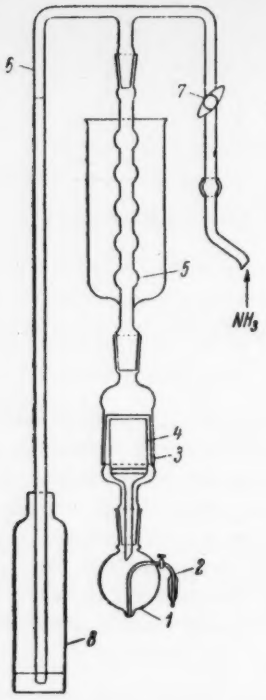

Fig. 1. Extractor.
1) Flask; 2) siphon; 3) conical connection; 4) funnel with glass filter; 5) condenser; 6) barometer tube; 7) stopcock; 8) mercury reservoir.

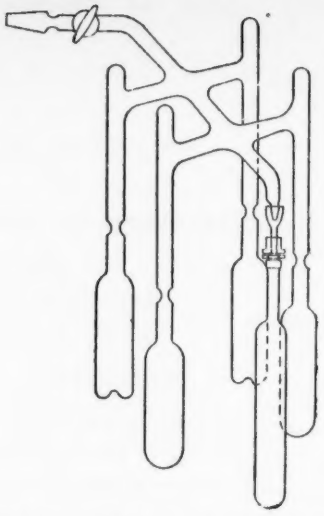

Fig. 2. Multiple collector for distilling deuterium solvents.

reaction between N_2H_4 and ND_3 occurred instantaneously [6]. After the deuteroammonia was distilled off, the deuterohydrazine was twice distilled over BaO in a high vacuum a multiple collector (Fig. 2) and was collected in ampoules with concave thinned bottoms, which were detached.

Anhydrous ethylenediamine was obtained in an analogous manner by ammonolysis of ethylenediamine sulfate. The latter was prepared by neutralizing a commercial 20% aqueous solution of ethylenediamine by concentrated sulfuric acid, evaporating the water, and drying the salt at 120° in a stream of nitrogen or hydrogen. Deuterium was introduced into the anhydrous ethylenediamine as described above.

Ethanol amine, a commercial preparation, was distilled over sodium. We collected the middle fraction for our work. Deuterium was introduced in the same way as for the other solvents.

Isotopic Analysis of the Solvents

Isotopic analysis of deuterium substituted ammonia, hydrazine, ethylenediamine, and ethanol amine consisted in burning 0.1-0.2 g of the substance and determining by the micro method [7] the deuterium concentration in the water obtained by the laboratory method of burning and purifying [8].

Hydrazine, ethylenediamine and ethanol amine were burned in a stream of oxygen by the method of rapid burning of organic substances worked out in this laboratory. Burning of ammonia was carried out over copper oxide at 700-750°. The water obtained by burning ammonia was distilled through the same oven with copper oxide and then purified.*

Examples of the analyses: deuterium substituted ammonia – 20.8, 20.5, 20.4, average 20.6 at. %; deuterium substituted hydrazine – 37.5, 37.7, 38.1, 37.9, average 37.8 at. %. Accuracy of the analysis ±1-2%.

*This method of isotopic analysis of ammonia, worked out by the authors of this paper, is used in all the work of our laboratory for the study of the reactions of hydrogen exchange with liquid deuteroammonia.

Method of Carrying out Experiments on Isotope Exchange

Solutions of organic substances in deuterohydrazine were prepared in a high vacuum. The collector (Fig. 3) was joined by a ground glass joint to the high vacuum apparatus. In an ampoule sealed to the collector was

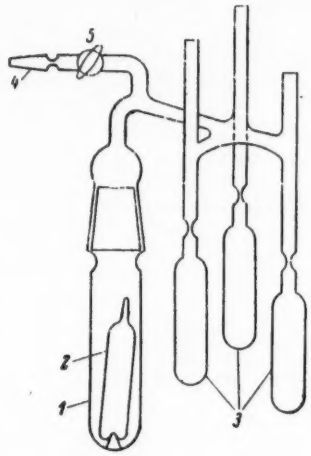

Fig. 3. Collector for preparing solutions in hydrazine.
1) Vessel with support;
2) ampoule with thin bottom, filled with solvent; 3) ampoule with substance; 4) joint for uniting to the vacuum apparatus; 5) stopcock.

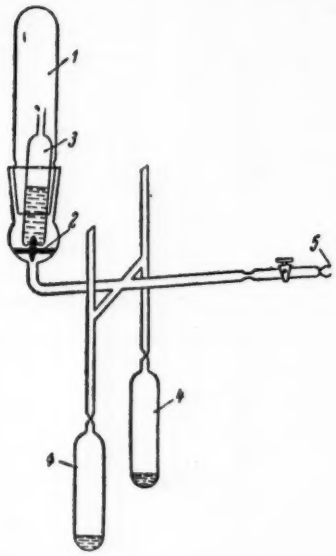

Fig. 4. Collector for preparing solutions with ethylenediamine.
1) Vessel; 2) support; 3) ampoule with solvent; 4) ampoule with substance;
5) joint for uniting with vacuum apparatus.

placed a weight of substance sufficient for obtaining about 0.2 g of water from it by burning, and on the support of vessel 1, joined to the connection, was placed ampoule 2 which was filled with deuterohydrazine. After pumping out, stopcock 5 was closed, the collector was disconnected from the high vacuum system and lightly shaken to break the bottom of ampoule 2. The whole ampoule was evenly cooled with liquid nitrogen including the sample of substance, then into each ampoule was distilled 5-6 grams of deuterohydrazine; the ampoule was detached and placed in a thermostat. After remaining in the thermostat, the ampoule was placed in a mixture of carbon dioxide and acetone and was opened; the hydrazine was distilled off in a high vacuum. The organic substance was washed with ammonia, alcohol, or water (depending on its properties) to guarantee full removal of deuterohydrazine. After the substance was dried in a vacuum, its constants were determined (melting point, refractive index), and then the substance was dried, the water which it formed was purified, and its concentration of deuterium was determined by the micromethod.

The solution of organic substances in deuteroethylenediamine was also prepared in a high vacuum. We introduced small changes in the construction of the apparatus which permitted flowing and not distilling the deuteroethylenediamine onto the sample of substance, which greatly shortened the experiment (10-15 min) at room temperature. In the collector used for this purpose (Fig. 4) vessel 1 was rotated 180° with respect to the ampoule. When the ampoule with the deuteroethylenediamine was placed on the support of vessel 1 and broken, the collector was twisted to pour the ethylenediamine into these ampoule, which was removed and placed in the thermostat. Separation of the substance from ethylenediamine in each case was different and was determined by the individual peculiarities.

The experiments with ethanol amine were carried out without special precautions. Ethanol amine was added to a weight of substance in air; the ampoule was pumped out and sealed. After the experiments the substance was separated from the ethanol amine by pouring into water, and filtering.

TABLE 2

Results of Experiments on Isotopic Exchange

τ min	C_s°	C_c°	C_c	α_p	k (sec^{-1})
			Fluorene-ammonia, 25°		
30	13.5	—	0.48	0.4	$1.4 \cdot 10^{-4}$
30	29.2	—	1.65	0.6	$2.2 \cdot 10^{-4}$
60	13.3	—	1.10	0.8	$1.6 \cdot 10^{-4}$
60	29.2	—	2.96	1.0	$2.2 \cdot 10^{-4}$
60	29.2	—	3.50	1.2	$2.0 \cdot 10^{-4}$
120	19.9	—	1.78	1.4	$2.0 \cdot 10^{-4}$
120	29.2	—	4.03	1.4	$2.0 \cdot 10^{-4}$
				Average	$2 \cdot 10^{-4}$
			Fluorene-ethylenediamine, 25°		
10	39.0	—	5.48	1.4	$2.4 \cdot 10^{-3}$
10	17.1	—	2.66	1.5	$3.0 \cdot 10^{-3}$
10	17.1	—	2.62	1.5	$3.0 \cdot 10^{-3}$
15	14.5	—	2.27	1.6	—
15	14.5	—	2.27	1.6	—
30	14.5	—	2.52	1.7	—
60	14.5	—	2.58	1.8	—
				Average	$3 \cdot 10^{-3}$
			Fluorene-ethanol amine, 25°		
15	—	3.11	2.58	—	$2.2 \cdot 10^{-4}$
15	—	3.11	2.48	—	$2.5 \cdot 10^{-4}$
15	—	3.11	2.48	—	$2.5 \cdot 10^{-4}$
30	—	3.11	2.00	—	$2.4 \cdot 10^{-4}$
30	—	5.00	2.75	—	$3.0 \cdot 10^{-4}$
30	56.7	—	4.21	0.74	$2.9 \cdot 10^{-4}$
90	7.8	—	0.88	1.12	$1.7 \cdot 10^{-4}$
				Average	$2 \cdot 10^{-4}$
			Triphenylmethane-ammonia, 120°		
105 hrs	29.2	—	0.16	0.09	$3 \cdot 10^{-7}$
105 "	29.2	—	0.12	0.07	$2 \cdot 10^{-7}$
168 "	29.2	—	0.18	0.10	$2 \cdot 10^{-7}$
168 "	29.2	—	0.16	0.09	$2 \cdot 10^{-7}$
168 "	29.2	—	0.17	0.09	$2 \cdot 10^{-7}$
				Average	$2 \cdot 10^{-7}$
			Triphenylmethane-hydrazine, 120°		
76 hrs	36.8	—	1.30	0.6	$(3 \cdot 10^{-6})$
96 "	27.7	—	0.75	0.4	$(2 \cdot 10^{-6})$
105 "	34.2	—	1.70	0.8	$(5 \cdot 10^{-6})$

TABLE 2 (continued)

τ, min	C_s^0	C_c^0	C_c	α_p	k (sec^{-1})
168	31.1	—	1.08	0.6	$(2 \cdot 10^{-6})$
168	31.1	—	1.14	0.6	$(2 \cdot 10^{-6})$
168	31.1	—	1.10	0.6	$(2 \cdot 10^{-6})$
200	36.8	—	1.51	0.7	$(2 \cdot 10^{-6})$
				Average	$2 \cdot 10^{-6}$
		Triphenylmethane-ethylenediamine, 120°			
50	39.0	—	0.58	0.2	$2 \cdot 10^{-6}$
79	39.0	—	0.97	0.4	$2 \cdot 10^{-6}$
80*	29.4	—	0.49	0.3	$1 \cdot 10^{-6}$
91	43.2	—	1.07	0.4	$2 \cdot 10^{-6}$
112*	29.4	—	0.66	0.4	$1 \cdot 10^{-6}$
				Average	$2 \cdot 10^{-6}$
		Triphenylmethane-ethanolamine, 120°			
103	56.7	—	0.57	0.16	$5 \cdot 10^{-7}$
121	19.7	—	0.18	0.15	$4 \cdot 10^{-7}$
124	56.7	—	0.84	0.24	$6 \cdot 10^{-7}$
157	19.7	—	0.28	0.23	$5 \cdot 10^{-7}$
				Average	$5 \cdot 10^{-7}$
100	—	0.67	0.57	—	$4 \cdot 10^{-7}$
100	—	0.67	0.57	—	$4 \cdot 10^{-7}$
109	—	5.27	4.69	—	$3 \cdot 10^{-7}$
162	—	5.27	4.27	—	$4 \cdot 10^{-7}$
162	—	5.27	4.44	—	$3 \cdot 10^{-7}$
				Average	$4 \cdot 10^{-7}$
		Diphenylmethane-ammonia, 120°			
200	90.9	—	0.06	0.008	$6 \cdot 10^{-9}$
200	90.9	—	0.07	0.009	$7 \cdot 10^{-9}$
				Average	$7 \cdot 10^{-9}$
		Diphenylmethane-hydrazine, 120°			
168	31.1	—	0.46	0.2	$(2 \cdot 10^{-7})$
200	36.8	—	0.77	0.3	$(2 \cdot 10^{-7})$
200	36.8	—	0.74	0.2	$(2 \cdot 10^{-7})$
200	36.8	—	0.55	0.2	$(2 \cdot 10^{-7})$
				Average	$2 \cdot 10^{-7}$

*Experiments were carried out with deuteroethylene diamine preparations repeatedly distilled over metallic potassium.

TABLE 2 (continued)

τ sec	C_s^0	C_c^0	C_c	α_p	k (sec^{-1})
			Diphenylmethane-ethylenediamine, 120°		
65	43.6	—	0.16	0.04	$1 \cdot 10^{-7}$
84	43.6	—	0.20	0.06	$1 \cdot 10^{-7}$
112	40.9	—	0.28	0.08	$1 \cdot 10^{-7}$
				Average	$1 \cdot 10^{-7}$
			Quinaldine-ethylenediamine, 120°		
79	22.3	—	2.30	0.9	$1 \cdot 10^{-6}$
109	42.8	—	5.27	1.1	$1 \cdot 10^{-6}$
151	42.8	—	6.50	1.4	$1 \cdot 10^{-6}$
				Average	$1 \cdot 10^{-6}$
			Quinaldine-ethanol amine, 120°		
5	56.7	—	2.05	0.3	$0.7 \cdot 10^{-5}$
7.5	56.7	—	2.45	0.4	$0.6 \cdot 10^{-5}$
10	19.7	—	1.00	0.5	$0.5 \cdot 10^{-5}$
15	19.7	—	1.58	0.7	$0.6 \cdot 10^{-5}$
5	—	1.08	0.89	—	$1 \cdot 10^{-5}$
6	—	1.08	0.81	—	$1 \cdot 10^{-5}$
12	—	1.08	0.67	—	$1 \cdot 10^{-5}$
12	—	1.08	0.70	—	$1 \cdot 10^{-5}$
109	—	1.08	0.10	—	—
162	—	1.08	0.07	—	—
162	—	1.08	0.07	—	—
				Average	$8 \cdot 10^{-6}$

The experiments on isotopic exchange with liquid deuteroammonia were carried out using the method worked out and often tested in our laboratory [4-9].

Characteristics of the Preparations

Fluorene. Twice recrystallized from alcohol. M. p. 115°. Deuterofluorene* was obtained by isotopic exchange with ND_3. C_s^0 = 17.3 at. %, C_c = 3.11 at. %, α_p = 1.8. Recrystallized from alcohol. M. p. 115°. Deuterium entered the methylene group. Triphenylmethane, Eastman Kodak preparation. M. p. 92°. Deuterotriphenylmethane* was obtained by decomposing $(C_6H_5)_3CK$ with heavy water. The salt was obtained by dissolving triphenylmethane in a mixture of NH_3 + KNH_2. Recrystallized from alcohol. M. p. 93°. The deuterium entered the methine group. Diphenylmethane from the Kharkov Khimreaktiv Factory. M. p. 26.5°. Quinaldine was vacuum distilled, $n^{20}D$ 1.6110. Picrate m. p. 193.5°. Deuteroquinaldine* substituted by deuterium in the methyl group was obtained by short isotopic exchange with a 0.1 N solution KND_2 in ND_3. C_s = 5.85 at. %, C_c = 1.08 at. %, α_p = 1.3. Twice redistilled in vacuum, $n^{20}D$ 1.6099.

Determination of Rate Constant of Isotopic Exchange

The results of the experiments on exchange are given in Table 2 where: τ is duration of experiment, C_s^0 is deuterium concentration in the solvent, C_c^0 is deuterium concentration in the compound before the experiment,

*See the note on page 1762. The abbreviations (C_s^0, C_c, α_p) are explained below.

C_c the deuterium concentration in the compound after the experiment, α_p the number of exchanged hydrogen atoms by distribution coefficient of deuterium between compound and solvent, $\underline{k}$ the rate constant calculated by the equation of the first order.

The values of $\underline{k}$ obtained in this work do not pretend to accuracy. The values of $\underline{k}$ obtained in the experiments with hydrazine have a purely conditional character and are placed in parentheses, since the experiments were carried out in a heterogeneous system because of the poor solubility of the organic substances in hydrazine.

The solubility of the organic substances with which this work was carried out in ethylenediamine was considerably better than in ammonia and ethanol amine. Solution of triphenylmethane and especially fluorene went slowly; this somewhat altered the results of the experiments on exchange. With a weight of compound in all cases of about 0.25 g, the weight of deuteroammonia and ethanol amine was about 15 g, of deuteroethylenediamine about 5 g, of deuterohydrazine, about 11 g. All the substances with which the work was carried out were not changed chemically during the exchange reaction, as indicated by the constancy of their constants before and after the experiments.

Measurement of the Rate of Isotopic Exchange in the Presence of Catalysts

Comparison of the catalytic activity of basic catalysts in the studied solvents and comparison of the rate of hydrogen exchange in different solvents with the same basic catalyst could be a further step in explaining the mechanism of the reaction of isotopic exchange of hydrogen.

Usually in the reaction of alkali metals with solvents, bases are obtained. Thus, alkali hydroxides, alcoholates and amides of the metals are formed in the reaction between the metals and, respectively, water, alcohol, and ammonia. Ethanol amine reacts with alkali metals to form $NH_2CH_2CH_2OK$ and $NH_2CH_2CH_2ONa$ which are easily soluble in it. In the reaction of alkali metals with anhydrous hydrazine unstable hydrazides are formed.

When anhydrous ethylenediamine is added in a vacuum to metallic potassium, the metal becomes blue on the surface and over several hours forms a blue solution. The solution is formed only under conditions of very careful drying of the ethylenediamine by repeatedly distilling it in a vacuum over metallic potassium. Potassium and sodium amides are poorly soluble in anhydrous ethylenediamine.* The color of the solutions became successively violet, yellow-green, and brown. The solution catalyzed the reverse reaction. Thus, at room temperature after 18 days there occurred almost full exchange of hydrogen in naphthalene and after 5 days half the atoms of hydrogen in its molecule had exchanged.

C_2H_5OK and $NH_2C_2H_4OK$ were also very weakly soluble in ethylenediamine.

Attempts to prepare a 0.1 N solution of C_2H_5OK in ethylenediamine led to formation of a yellow solution, but most of the C_2H_5OK remained undissolved. Experiments on the exchange of hydrogen in triphenylmethane with this solution showed that the methine atom exchanged hydrogen already in 15 min even at 25°, while without a catalyst the exchange became noticeable only at 120° ($k = 2 \cdot 10^{-6}$, see Table 2).

Analogous results were obtained with 0.1 N solutions of $H_2NCH_2CH_2OK$ in ethylenediamine.

The same bases, but dissolved correspondingly in ethanol amine and ethyl alcohol showed a much lower catalytic activity. This follows from the results of Table 3 and of the experiments of E. N. Zviagintseva [11] which showed that at 120° a 1 N solution of C_2H_5OK in C_2H_5OD caused hydrogen exchange in triphenylmethane with a rate of $3 \cdot 10^{-5}$ sec^{-1}.

DISCUSSION OF RESULTS

The results of measuring the rate constants of hydrogen exchange are given in Table 4.

As Table 4 shows, hydrogen exchange with deuterohydrazine and deuteroethylenediamine occurs more rapidly than with deuteroammonia. The results of the experiments with hydrazine are particularly convincing because the exchange of hydrogen between triphenyl and diphenylmethane and hydrazine, is distinction from ammonia, takes

* KNH_2, C_2H_5OK, and $NH_2C_2H_4OK$ were obtained by reaction of the metal with the corresponding solvent and after evaporation of the solvent, the dry residue was treated in a vacuum with ethylenediamine.

TABLE 3

Hydrogen Exchange with Ethanol Amine with a $NH_2C_2H_4O^-$ Catalyst

τ hrs.	C_s^*	C_c^*	C_c	α_p	k(sec^{-1})
Fluorene, 0.1 N $NH_2C_2H_4OK$, 25°					
0.25	—	5.00	0.41	—	$2.8 \cdot 10^{-3}$
0.25	—	5.00	0.50	—	$2.3 \cdot 10^{-3}$
0.50	—	5.00	0.29	—	$1.6 \cdot 10^{-3}$
				Average	$2 \cdot 10^{-3}$
Triphenylmethane, 0.1 N $NH_2C_2H_4OK$, 120°					
5	—	2.02	1.41	—	$2.0 \cdot 10^{-5}$
10	—	2.02	0.97	—	$2.0 \cdot 10^{-5}$
15	—	2.02	0.89	—	$1.5 \cdot 10^{-5}$
12	7.84	—	0.32	0.65	$2.8 \cdot 10^{-5}$
				Average	$2 \cdot 10^{-5}$
Triphenylmethane, 0.01 N $NH_2C_2H_4OK$, 120°					
15	—	1.85	1.47	—	$4 \cdot 10^{-6}$
10	—	1.85	1.65	—	$3 \cdot 10^{-6}$
9	—	1.85	1.74	—	$2 \cdot 10^{-6}$
7.3	—	5.27	4.57	—	$6 \cdot 10^{-6}$
6.3	—	5.27	4.56	—	$6 \cdot 10^{-6}$
6	—	5.27	5.05	—	$2 \cdot 10^{-6}$
6	—	5.27	5.05	—	$2 \cdot 10^{-6}$
				Average	$4 \cdot 10^{-6}$

TABLE 4

Rate Constants of Hydrogen Exchange

Substance	k (sec^{-1}) (120°)			
	ND_3	N_2D_4	$ND_2C_2H_4ND_2$	$ND_2C_2H_4OD$
Fluorene**	$2 \cdot 10^{-4}$ ***	—	$3 \cdot 10^{-3}$	$2 \cdot 10^{-4}$
Triphenylmethane	$2 \cdot 10^{-7}$	$(2 \cdot 10^{-6})$	$2 \cdot 10^{-6}$	$4 \cdot 10^{-7}$
Diphenylmethane	$7 \cdot 10^{-9}$	$(2 \cdot 10^{-7})$	$1 \cdot 10^{-7}$	—
Quinaldine	$7 \cdot 10^{-8}$ ****	—	$1 \cdot 10^{-6}$	$8 \cdot 10^{-6}$

*In the experiments with fluorine, the rate constant was measured at 25°.

**The rate constants obtained in [10] are lower, evidently because of the incomplete solubility of fluorene which was not noticed since the experiments were carried out in metal ampoules.

***Measured by E. N. Zviagintseva [11].

place in a heterogeneous system. The more rapid exchange of deuterium with hydrazine, a weaker base, than with ammonia is evidently related to the fact that the DC of hydrazine is 3 times greater than the DC of ammonia and its molecules are more polar.

The DC of ammonia and ethylenediamine are very close. Therefore the greater rate of exchange (by 10-15 times) with the second solvent must naturally be ascribed to its very protophilic nature. It is possible that the

greater polarity of the ethylenediamine molecule also plays an important part.*

Deuterium exchange with ethanol amine shows characteristic peculiarities. The hydrogen of the methylene group of fluorene and the methine group of triphenylmethane exchanges with ethanol amine at about the same rate as with liquid ammonia, while the hydrogen of the methyl groups of quinaldine exchanges with ethanol amine more than twice as fast as with ammonia. In order to understand the reason for such contradictory results, we had to compare the rate of exchange in these substances with ammonia and ethanol. It has been shown [11] that hydrogen exchange between liquid ammonia and fluorene occure 6 times faster than with alcohol, while exchange of quinaldine with alcohol is faster than with ammonia. This was explained by different mechanisms of hydrogen exchange in these compounds.

The presence of two functional groups in the ethanol amine molecule permits it to act in two ways. We assume that in isotopic exchange of hydrogen in the CH_2 groups of fluorene, in the first step the amino group nitrogen of ethanol amine is the proton acceptor, while in the reaction with quinaldine a hydrogen bond is formed between the quinaldine nitrogen atom and the hydroxyl group of the ethanol amine, and the nitrogen acquires a positive charge. This leads to a decreased electron density on the carbon atom with which the methyl group is united, and in turn this eases the protonization of the hydrogen atom in the latter. We may think that the nitrogen atom of another ethanol amine molecule acts as proton acceptor. The greater protophilic character of ethanol amine as compared to quinaldine, which we must assume to play the part of acceptor in exchange in alcohol solution, is the reason for the fact that the rate of the exchange reaction in ethanol amine ($k = 8 \cdot 10^{-6}$) and in ammonia ($k = 7 \cdot 10^{-8}$) differs more than in alcohol ($k = 7 \cdot 10^{-7}$) and ammonia.

Table 5 gives the rate constants for the exchange of hydrogen in the methine group of triphenylmethane with the solvents and catalysts which interest us.

TABLE 5

Rate of Hydrogen Exchange in Triphenylmethane

Solvent	Catalyst	Temperature	k (sec^{-1})
Ethanol amine	—	120°	$4 \cdot 10^{-7}$
Ethylenediamine	—	120	$2 \cdot 10^{-6}$
Ethanol amine	$NH_2C_2H_4OK$, ~0.01 N	120	$3 \cdot 10^{-6}$
Ethanol amine	$NH_2C_2H_4OK$, ~0.1 N	120	$2 \cdot 10^{-5}$
Ethylenediamine	$NH_2C_2H_4OK$, < 0.1 N	25	$> 10^{-3}$
Ethanol	C_2H_5OK, 1 N	120	$3 \cdot 10^{-5}$
Ethylenediamine	C_2H_5OK, < 0.1 N	25	$> 10^{-3}$

As the results in Table 5 show, the rate constants for the exchange reaction with ethylenediamine are about 5 times greater than with ethanol amine. At the same time, if the same catalyst ($NH_2C_2H_4OK$) is dissolved in these two solvents, the difference in rate constants is not less than 4-5 times, if we calculate that the experiments with ethylenediamine were carried out at a temperature 95° lower than those with ethanol amine.

A similar picture is found in comparing the rate of the exchange reactions which are catalyzed by alcoholates in ethanol and ethylenediamine.

Thus, a change in solvent can be very strongly reflected in the catalytic activity of the same base** in the reaction of isotopic exchange of hydrogen. It is interesting to compare with this the finding made in another study [11], that potassium hydroxide causes metallation of hydrocarbons dissolved in liquid ammonia.

We hope to study the rate of the exchange reactions catalyzed by the same base and in different solvents.

* We once more emphasize the very conditional and unreliable estimates of the relative strengths of the solvents as based on the K_{H_2O} values, which we must use because of the absence of reliable methods of comparison.

** We assume that the degree of transformation of alcoholate into $NH_2C_2H_4NH^-$ is very slight, since ethylenediamine is much more strongly basic than alcohol.

We express thanks to Iu. Bakshi who participated in carrying out the experiments with solutions in ethylenediamine in the absence of catalysts.

SUMMARY

1. We have described the preparation of anhydrous deuterium substituted hydrazine, ethylenediamine, and ethanol amine, methods for their isotopic analysis, and the performance of experiments on isotopic exchange of hydrogen with them.

2. We have measured the rate of isotopic exchange of hydrogen in fluorene, triphenylmethane, diphenylmethane, and quinaldine with these solvents and with liquid ammonia.

3. We have discussed the reasons for the high rate of hydrogen exchange with hydrazine and ethylenediamine compared to liquid ammonia.

4. The peculiarities of deuterium exchange with ethanol amine have been explained by the fact that it can act as a donor and an acceptor of protons (deuterons).

5. We have measured the rate of isotopic exchange of hydrogen in triphenylmethane with ethylenediamine with catalysis by ions of $C_2H_5O^-$ and $NH_2C_2H_4O^-$, and also with ethanol amine with catalysis by $NH_2C_2H_4O^-$ ions. We have shown that the catalytic activity of a base depends in very great degree on the nature of the solvent.

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STUDIES OF THE REACTIONS OF TITANIUM TETRACHLORIDE WITH ESTERS OF MONOBASIC ACIDS

XII. THE DECOMPOSITION OF THE COMPOUNDS $TiCl_4 \cdot$ ESTER

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In our previous investigations [1-6] we established that titanium tetrachloride dissolves in esters of monobasic acids to form compounds of the composition $TiCl_4 \cdot E$ and $TiCl_4 \cdot 2E$ (where E is a molecule of ester); the product $TiCl_4 \cdot E$ is stable in the liquid phase and exists without change over a wide temperature interval. We did not find formation in the liquid phase of the compound $2TiCl_4 \cdot E$ which Demarcay [7] obtained by fusing exactly calculated amounts of the components. Although our data indicate the considerable stability of most esters to the action of titanium tetrachloride [1-6], there is information in the literature [8-15] about the splitting of ethers and esters in the presence of halides of aluminum and other metals which permits the assumption of an analogous reaction for some of the ester derivatives of titanium tetrachloride. Starting from the results of investigations of the decomposition of aluminum etherates [12-14], we assumed that the decomposition of the ester derivatives of titanium tetrachloride might occur when the esters which reacted with $TiCl_4$ consisted of strong acid residues and alcohol radicals with low electronegativity. This condition is satisfied by isopropyl formate, benzyl formate, and others [16], and the compound of $TiCl_4$ with the corresponding esters of trichloroacetic acid should tend to split even more easily.

According to ideas of polarization, among compounds of the types $TiCl_4 \cdot 2E$, $TiCl_4 \cdot E$, and $2TiCl_4 \cdot E$, most rapid decomposition would be expected in compounds of the last two types.

In the present work we give results of a study of the reaction of titanium tetrachloride with esters of the above structures. We also tested the results of Demarcay [7] on the compound $2TiCl_4 \cdot E$, whose existance we had not confirmed in the liquid phase, in order to explain its role in the decomposition of esters under the influence of titanium tetrachloride.

EXPERIMENTAL

The esters, synthesized by the esterification reaction, after purification and drying [2-6] were fractionally distilled since the boiling point, refractive index, and density had not agreed with the literature data. Titanium tetrachloride was the same as in previous work [2-6]. As the solvent for obtaining the compounds we used carefully dried benzene. For washing the crystals which were obtained by mixing benzene solutions containing the calculated amounts of components, we used benzene and methylene chloride. The resulting washed and filtered compounds were placed in an apparatus which permitted carrying out operations without admitting moisture. The dry compounds were placed in a container with a stopcock and the air was pumped out. We used our method for determining titanium as TiO_2 (precipitated by ammonia) and we determined chloride by the Volhard method; these are recommended for analysis of similar compounds [17].

Compounds $TiCl_4 \cdot E$ and $2TiCl_4 \cdot E$

As Table 1 shows, the compounds formed from solutions of titanium tetrachloride in esters of trichloroacetic acid have the equimolecular composition. They are unstable yellow crystals which dissociate into the starting compounds when they melt [6]. Due to their low melting points, we did not succeed in isolating the compounds $TiCl_4 \cdot$ n-$CCl_3COOC_4H_9$ and $TiCl_4 \cdot$ iso-$CCl_3COOC_5H_{11}$, even with cooling to $-20°$. Although the compounds $TiCl_4 \cdot CCl_3COOC_2H_5$ and $TiCl_4 \cdot CCl_3COO$ iso C_4H_9 easily dissociate into their components [6], decomposition of the esters was not found here. On the other hand, the compound $TiCl_4 \cdot$ iso-$CCl_3COOC_3H_7$ when

weakly heated, splits energetically with the formation of products which indicate decomposition of the ester. The same result is found with the compound $TiCl_4 \cdot$ iso-$HCOOC_3H_7$, but the decomposition in this case begins at a higher temperature.

To test the existence of compounds $2TiCl_4 \cdot E$ we studied the reaction of titanium tetrachloride with esters of benzoic acid, since, according to the data of Demarcay [7], the most stable compounds of this type were obtained by him by melting the calculated amounts of $TiCl_4$ with methyl and ethyl benzoate.

As Table 1 shows, when benzene solutions which contained equimolecular amounts of the components were mixed, the compounds formed had a 1:1 ratio.

TABLE 1

Compound	Calculated (in wt. %)		Found (in weight %)	
	Ti	Cl	Ti	Cl
$TiCl_4 \cdot Cl_3CCOOC_2H_5$	12.56	—	12.47, 12.57	—
$TiCl_4 \cdot$ iso-$Cl_3CCOOC_3H_7$	12.12	—	12.66, 12.28	—
$TiCl_4 \cdot$ iso-$Cl_3CCOOC_4H_9$	11.70	—	11.78, 11.68	—
$TiCl_4 \cdot$ n.-$HCOOC_3H_7$	17.24	51.05	17.22, 17.29	50.87, 51.31
$TiCl_4 \cdot C_6H_5COOC_2H_5$	14.09	41.72	14.14, 14.12	41.87, 41.82
$TiCl_4 \cdot$ iso-$C_6H_5COOC_4H_9$	13.02	38.54	13.36, 13.28	39.50, 39.24
$TiCl_4 \cdot$ iso-$C_6H_5COOC_5H_{11}$	12.54	37.13	12.75, 12.69	37.65, 37.51
$HCOOTiCl_3$	24.03	53.37	24.10, 24.11	53.23, 53.30
$Cl_3CCOOTiCl_3$	15.12	—	15.21, 15.20	—

TABLE 2

Compound	Titanium content (in weight %)		
	calculated	found	
		without washing	after washing with C_6H_6
$2TiCl_4 \cdot CH_3COOC_2H_5$	20.49	21.32, 21.22	17.42
$2TiCl_4 \cdot C_6H_5COOC_2H_5$	18.09	18.83, 18.88	14.33
$2TiCl_4 \cdot$ n.-$C_6H_5COOC_4H_9$	17.18	17.99, 17.96	13.39
$2TiCl_4 \cdot$ iso-$C_6H_5COOC_5H_{11}$	16.75	17.41, 17.51	12.78

The compound $TiCl_4 \cdot E$ crystallized from benzene solutions which contained $TiCl_4$ and the ester in the ratio 2:1. The same result was obtained using methylene chloride or carbon tetrachloride as solvents. Since we did not succeed in isolating the compound $2TiCl_4 \cdot E$ from solution, we tried to obtain it by adding a small amount of ester to an excess of titanium tetrachloride (0.2 g-mole of ester to 1 g-mole of $TiCl_4$). The results are shown in Table 2 which indicate that the crystals isolated from excess $TiCl_4$ have a composition close to a compound with ratio 2:1. However, even careful washing with benzene leads to decomposition of these compounds. The same result is obtained by washing with carbon tetrachloride and methylene chloride. Carbon tetrachloride and benzene do not react with titanium tetrachloride at room temperature [18, 19]; therefore the results allow us to conclude that the compound $2TiCl_4 \cdot E$, which can be considered to be formed by combination of $TiCl_4 \cdot E$ with $TiCl_4$, has slight stability, because of the high dipole moment of this compound [20].

Decomposition of Compounds $TiCl_4 \cdot E$

To determine the direction of decomposition of the compounds $TiCl_4 \cdot$ iso-$CCl_3COOC_3H_7$ and $TiCl_4 \cdot$ iso-$HCOOC_3H_7$ we studied the volatile products which were evolved.

Decomposition of the compound $TiCl_4 \cdot$ iso-$HCOOC_3H_7$ began at 60-70° and some excess of $TiCl_4$ favored this process. In the volatile products of the decomposition we noted besides $TiCl_4$ and $HCOOC_3H_7$, hydrogen

chloride, carbon monoxide, and a liquid which burned with a blue flame and whose vapor condensed in a trap cooled by solid carbon dioxide. The vapors of such a liquid were also found in the decomposition of $TiCl_4 \cdot iso\text{-}CCl_3COOC_3H_7$, which occurred more energetically and began at 30-35°. We did not find evolution of carbon monoxide in this case. The liquid formed in the decomposition conformed in its properties (characteristic odor, absence of reaction with bromine water) with isopropyl chloride. This was confirmed by the formation of isopropyl benzene by passing the vapors of the liquid through benzene which contained $AlCl_3$.

The results of the analysis of the nonvolatile products which remained after the decomposition, red-brown in the case of splitting of $TiCl_4 \cdot iso\text{-}CCl_3COOC_3H_7$, and gray in the case of the decomposition of $TiCl_4 \cdot iso\text{-}HCOOC_3H_7$, are given in the last two columns of Table 1.

The data permit us to conclude that the compounds $TiCl_4 \cdot E$ decompose by a reaction analogous [12-14] to that for aluminum trichloride: $TiCl_4 \cdot RCOOR' \rightarrow R'Cl + RCOOTiCl_3$, and in the case of formates there is partial further decomposition: $HCOOTiCl_3 \rightarrow HCl + CO + TiOCl_2$ and $TiOCl_2 \rightarrow TiCl_4 + TiO_2$.

We found that when $HCOOTiCl_3$ was heated, carbon monoxide, hydrogen chloride, $TiCl_4$, and TiO_2 were formed, which confirmed our assumption.

The decomposition of the compounds with ratio 1 : 1 formed from titanium tetrachloride with benzyl formate and especially with benzyl trichloroacetate occurred with warming and was so violent that it was not possible to isolate the compounds $TiCl_4 \cdot E$ though their formation was indicated by the appearance of a dark red color when equimolecular amounts of the components were mixed. The decomposition of these compounds was accompanied by violent evolution of hydrogen chloride and formation of a yellow tar insoluble in alcohol and ether, but easily soluble in chloroform and benzene. Decomposition of $TiCl_4 \cdot CH_3COOCH_2C_6H_5$ goes with evolution of hydrogen chloride and formation of the yellow tar, but the process in this case requires heating to 100-150° and goes less energetically.

Formation of a yellow tar was observed in the action of $SnCl_4$ on ethers and esters of benzyl alcohol, and also directly on benzyl chloride. The composition of the yellow product could conform to the formula C_7H_6 [21, 22]. The tar formed by this process [22] and formed in our experiments both have the formula C_7H_6. Some variation of the analytical data from the calculated value is explained by the difficulty in separating the product from benzene.

Analysis of the tar formed from $TiCl_4 \cdot HCOOCH_2C_6H_5$.

Found %: C 92.52, 92.57; H 7.00, 6.93. C_7H_6. Calculated %: C 93.29; H 6.71.

Analysis of the tar formed from $TiCl_4 \cdot CCl_3COOCH_2C_6H_5$.

Found %: C 92.67, 92.79; H 6.91, 7.05. C_7H_6. Calculated %: C 93.29; H 6.71.

Analysis of the tar formed from $TiCl_4 \cdot CH_3COOCH_2C_6H_5$.

Found %: C 92.97, 92.61; H 6.88, 7.04. C_7H_6. Calculated %: C 93.29; H 6.71.

Thus the results confirm the assumption of the decomposition of the compounds $TiCl_4 \cdot E$ with formation of the product $RCOOTiCl_3$ and alkyl halides, and in the case of separation of benzyl chloride, the process is complicated by its condensation with the formation of the hydrocarbon C_7H_6.

The finding of hastening of the decomposition of these compounds by addition of excess $TiCl_4$ can be explained by partial formation of the unstable compound $2TiCl_4 \cdot E$.

SUMMARY

1. We have established that titanium tetrachloride gives compounds with a 1 : 1 ratio with esters of trichloroacetic or benzoic acids.

2. We have confirmed the existence in the solid phase of the compounds $2TiCl_4 \cdot E$ and shown the instability of the bond of the second molecule of $TiCl_4$ with $TiCl_4 \cdot E$.

3. We have shown that some compounds $TiCl_4 \cdot E$ can decompose in the same way as etherates of aluminum trichloride and explained the conditions of the decomposition.

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TERNARY CONJUGATE SYSTEM OF LITHIUM AND SODIUM BUTYRATES AND NITRATES

N. M. Tsindrik and N. M. Sokolov

The present work was undertaken with the purpose of showing the direction of exchange reaction between fused sodium and lithium butyrates and nitrates. It is interesting to compare this system with the previously studied systems of lithium and sodium formates, acetates, propionates and nitrates of the same metals.

EXPERIMENTAL

The liquidus surface of the system was studied by a visual-polythermal method. A nichrome-constantan thermocouple and a millivoltmeter were used to measure the temperatures at which first crystals appeared. Addition of excess butyric acid to a solution of chemically pure carbonates, followed by evaporation, produced lithium and sodium butyrates [1]. The dry salts obtained were then purified by recrystallization from butanol.

The melting points of the components in our systems were: $LiNO_3$ 256°, $NaNO_3$ 308°, C_3H_7COOLi 329°, C_3H_7COONa 330°. A polymorphic transition of sodium nitrate is known at 275°. For sodium butyrate polymorphic transitions were determined at 117, 232, 252, and 316° [2].

Side Faces (Table 1, Fig. 1)

1. $LiNO_3-NaNO_3$ system has been investigated by many authors. The components form a eutectic mixture. According to our data the eutectic point is at 198° and 45% sodium nitrate.

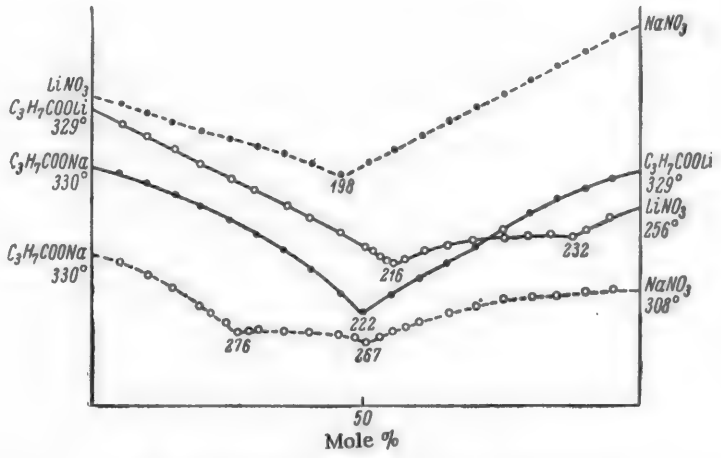

Fig. 1. Melting point curves of binary systems.

2. $LiNO_3-C_3H_7COOLi$ system was studied for the first time. The three branches of the melting curve intersect at 232° and 15%, 216° and 45% of C_3H_7COOLi. The probable composition of the compound is $7LiNO_3 \cdot C_3H_7COOLi$.

TABLE 1

Binary Systems

$LiNO_3$—$NaNO_3$		$LiNO_3$—C_3H_7COOLi		C_3H_7COOLi—C_3H_7COONa		C_3H_7COONa—$NaNO_3$	
Mole % of $NaNO_3$	Temp.	Mole % of C_3H_7COOLi	Temp.	Mole % of C_3H_7COONa	Temp.	Mole % of $NaNO_3$	Temp.
0	256°	0	256°	0	329°	0	330°
5	250	5	248	5	326	5	325
10	242	10	242	10	318	10	316
15	236	12.5	238	15	308	15	306
20	230	15	232	20	298	20	294
25	224	17.5	232	25	285	22.5	286
30	216	20	232	30	273	25	280
35	210	25	230	35	260	26.5	276
40	204	30	230	40	248	27.5	276
45	198	35	226	45	234	30	276
50	208	40	224	50	222	35	274
55	219	42.5	220	55	240	40	274
60	230	45	216	60	254	45	270
65	240	50	228	65	270	47.5	268
70	250	55	238	70	280	50	267
75	260	60	248	75	292	52.5	274
80	270	65	258	80	302	55	278
90	290	70	268	85	312	60	284
95	300	75	278	90	320	65	290
100	308	80	288	95	327	70	292
		85	298	100	330	75	296
		90	308			80	300
		100	329			90	304
						100	308

3. C_3H_7COOLi—C_3H_7COONa system was also studied for the first time. The eutectic point is at 222° and 50% C_3H_7COONa.

4. C_3H_7COONa—$NaNO_3$ system was previously described [3]. The three branches of the melting curve have eutectic points at 276° and 28%, 267° and 50% sodium nitrate. Probable composition of the compound is $3C_3H_7COONa \cdot NaNO_3$.

Diagonal Sections (Table 2, Fig. 2)

Stable diagonal section of $NaNO_3$—C_3H_7COOLi points to an irreversible process. The melting curve consists of two branches which intersect at 298° and 9% $NaNO_3$. From 10 to 97.5% of sodium nitrate phase-separation is observed.

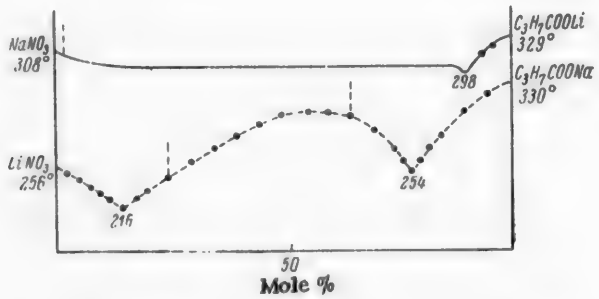

Fig. 2. Diagonal sections of ternary conjugate systems.

Unstable diagonal section $LiNO_3-C_3H_7COONa$ is made up of three branches ($LiNO_3$, C_3H_7COONa, and a branch of exchange product) which intersect in two places: 216° and 16%, 254° and 78% C_3H_7COONa. Phase-separation takes place in this section from 25 to 79% of C_3H_7COONa.

Internal Sections

We investigated 25 internal sections to find the surfaces of crystallization fields in the system; the directions of these sections are shown in Fig. 3, and their characteristics given in Figs. 4 and 5.

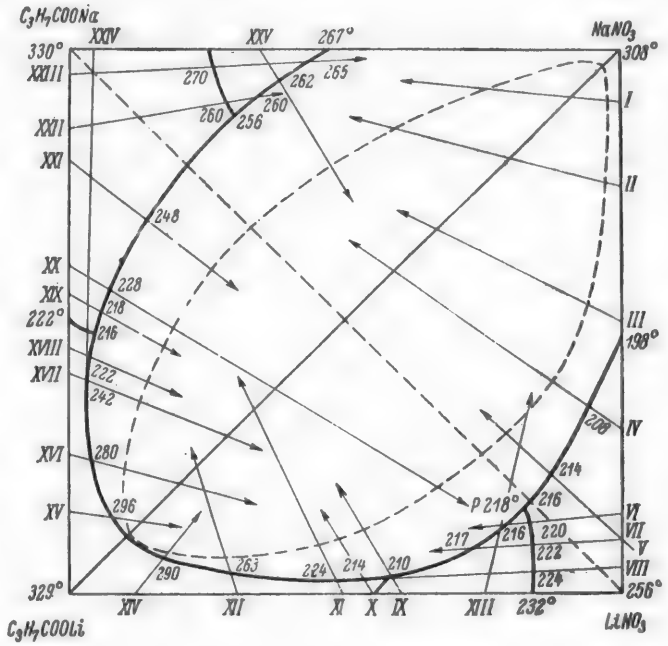

Fig. 3. Directions of internal sections.

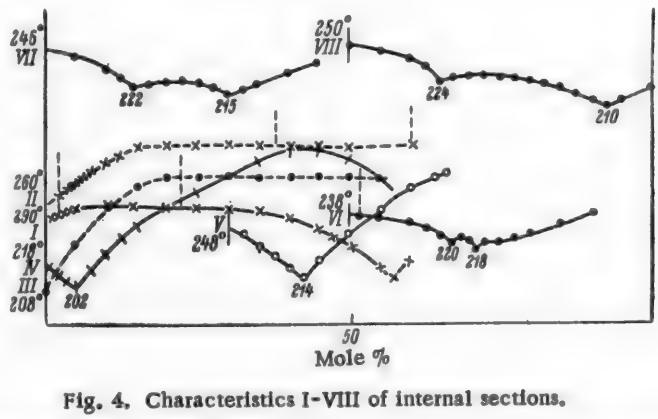

Fig. 4. Characteristics I-VIII of internal sections.

Using the results of our investigation of binary systems and internal sections, we projected the three-dimensional crystallization surfaces onto a square composition diagram (Fig. 6). The surface of the liquidus system consists of 6 fields. $NaNO_3$ field occupies 77.96%; $LiNO_3$, 5.37%; C_3H_7COONa, 9.05%; C_3H_7COOLi, 4.19%; $7LiNO_3 \cdot C_3H_7COOLi$, 2.21%; and $3C_3H_7COONa \cdot NaNO_3$, 1.22% of the total surface. Phase separation is located along the

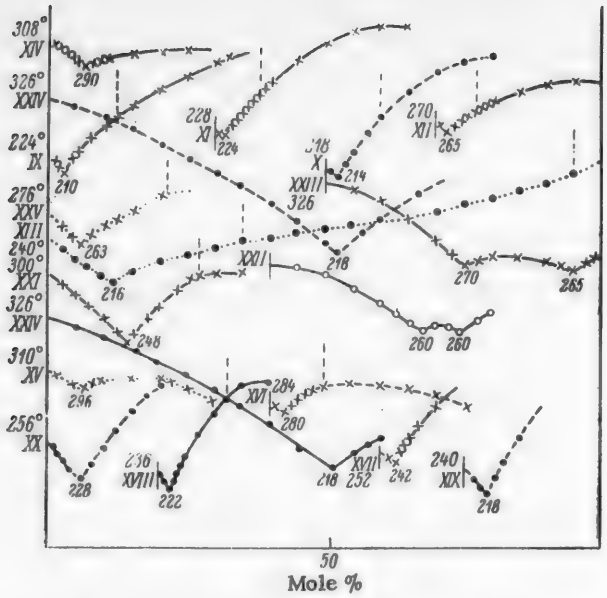

Fig. 5. Characteristics IX-XXV of internal sections.

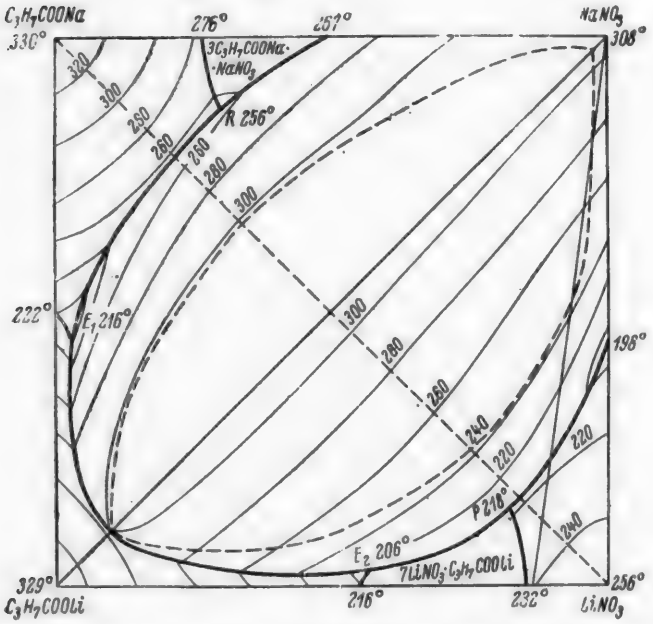

Fig. 6. Projection of a conjugate system diagram onto a composition square.

stable diagonal section in the form of a lens on the sodium nitrate field and occupies 66% of its area or 51.5% of the total liquidus surface area. The ternary eutectic curves intersect in two eutectic points, and in two other invariant points, which are of Type 1 and Type 2, respectively (at which one and two, respectively, of the three invariants lines fall to the invariant point and the others rise). Temperatures and compositions are listed in Table 3.

TABLE 2

Diagonal Sections

$C_3H_7COOLi-NaNO_3$		$C_3H_7COONa-LiNO_3$	
Mole % of C_3H_7COOLi	Temperature	Mole % of $LiNO_3$	Temperature
0	308°	0	330°
1	304	5	324
2.5	300	10	304
5	300	15	284
25	300	17.5	272
50	300	20	260
90	300	21	254
91	298	22.5	260
92.5	302	25	272
94	308	27.5	282
96	318	30	292
98	324	35	300
100	329	50	300
		55	296
		60	284
		70	258
		80	230
		82.5	222
		85	216
		87.5	224
		90	234
		95	246
		100	256

TABLE 3

Point	Type of point	Temp.	Composition (in mole %)			
			$LiNO_3$	$NaNO_3$	C_3H_7COONa	C_3H_7COOLi
E_1	Eutectic	216°	—	4	44	52
E_2	Eutectic	206	57.5	2.5	40	—
P	Type 1	218	67.5	14	—	18.5
R	Type 2	256	—	30	58	12

Figure 7 shows the location of invariant points and ternary eutectic lines projected on the $C_3H_7COOLi-LiNO_3$ side.

The stable diagonal section and the one leading from the supposed terminal of compound $7LiNO_3 \cdot C_3H_7COOLi$ to the top of $NaNO_3$ separate the square surface of the system into three-phase triangles: $NaNO_3-C_3H_7COONa-C_3H_7COOLi$, $NaNO_3-C_3H_7COOLi-$compound $7LiNO_3 \cdot C_3H_7COOLi$, $NaNO_3-$compound $7LiNO_3 \cdot C_3H_7COOLi-LiNO_3$.

We have previously investigated the conjugate formate, acetate, propionate and nitrate systems of lithium and sodium [4]. All these systems are of the diagonal type. Sodium nitrate and lithium salts of fatty acids form stable salt-pairs.

When the same geometrical elements of various systems [5] (stable diagonals and stable triangles) are compared, one observes that with increase in the number of carbon atoms in the radical the degree of equilibrium displacement increases.

SUMMARY

1. The liquidus surface of a ternary conjugate system of lithium and sodium butyrates and nitrates was studied for the first time.

2. The data on two binary systems: $LiNO_3-C_3H_7COOLi$ and $C_3H_7COOLi-C_3H_7COONa$ are reported for the first time.

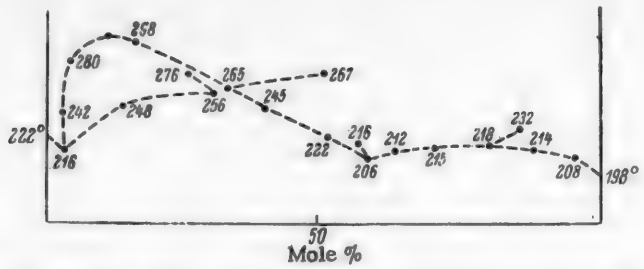

Fig. 7. The eutectic line projected on $C_3H_7COOLi-LiNO_3$ side.

3. The dependence of chemical equilibrium shift on the number of carbon atoms in the fatty acid radical was determined for a series of systems; the systems were those of formates, acetates, propionates, and butyrates and nitrates of lithium and sodium.

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NEW REGULARITIES IN THE PHYSICOCHEMICAL PROPERTIES OF HYDROCARBONS. II*

V. M. Tatevskii and V. A. Benderskii

In preceeding papers [1-3] we have shown that a series of hydrocarbon properties (those properties which as a rule contain capacity factors, for example: molar volume V, molar refraction R, heat of formation from atoms $\Delta H_{(at.)}$ or elements $\Delta H_{(el.)}$, heat of combustion $\Delta H_{(comb.)}$, heat of vaporization L, logarithm of the vapor pressure log p et al.), when converted to molar units are a linear function of the number (n) of carbon atoms in the hydrocarbon molecule. According to the theoretical ideas previously developed by us [1, 3], this linearity should be observed for specific hydrocarbon groups with the same structure in the branched sections of the hydrocarbon chain.

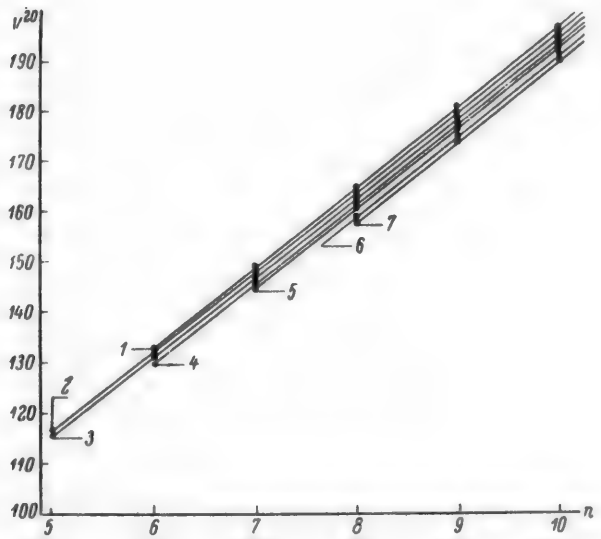

Fig. 1. Molar volumes V^{20} as a function of the number of carbon atoms (n) in alkane molecules of various groups.
1) 2,2-Dimethylalkanes; 2) 2-methylalkanes; 3) n-alkanes; 4) 3-methylalkanes; 5) 3,3-dimethylalkanes; 6) 3,4-dimethylalkanes; 7) 2,3,3-trimethylalkanes.

*For communication I see [3].

Values of Constants $\alpha^{(m)}$ and $\beta^{(m)}$ for Various Physicochemical Properties of Some Homologous Alkane Groups

Alkane group	$V^{(20)}$ ml/mole		$\Delta H_{(el.)}$ (kcal/mole)		$L^{\circ}_{vap.}$ (kcal/mole), t = 130-170°		Log P_{60} (mm of Hg)		$d_4^{(20)}$			t_b		
	α	β	α	β	α	β	α	β	A	B	n_0	t_0	B	n_0
n-Alkanes	34.04	16.108	—10.25	—4.95	1750	857	5.322	—0.428	0.8496	—1.2875	0.7647	782.18	16402	17.98
2-Methylalkanes	37.02	15.838	12.58	4.86	1843	811	5.401	—0.421	0.8526	—1.3795	0.92	822.93	18724	18.55
3-Methylalkanes	33.31	16.069	—11.57	—4.91	2041	784	5.307	—0.412	0.8682	—1.5915	1.8	934.97	25591	23.56
3-Ethylalkanes	29.76	16.270	— 9.92	5.06	—	—	5.084	—0.383				2683.02	265104	95.38
2,2-Dimethyl-alkanes	37.40	15.888	16.36	4.68	1516	789	5.452	—0.406	0.8548	—1.4224	0.9172	983.95	28701	24.72
2,3-Dimethyl-alkanes	30.63	16.22	23.05	3.51	1805	791	5.184	—0.389	0.8503	—1.2410	1.0	1246.52	50390	36.56
2,4-Dimethyl-alkanes	31.90	16.38	—	—	—	—	—	—						
3,3-Dimethyl-alkanes	32.84	15.98	17.09	4.44	1604	792	5.201	—0.383				1603.43	87344	50.56
3,4-Dimethyl-alkanes	31.41	15.95	—	—	—	—								
2,(n-1)Dimethyl-alkanes	37.00	15.98	13.93	4.91	581	921	5.569	—0.425				818.62	18380	17.90
2,2,(n-1)-Tri-methylalkanes	34.99	15.98	—	—	785	840	6.879	—0.562						
2,2,3,3-Tetra-methylalkanes	20.00	16.61	—	—	—	—								

In the present work it is shown that theoretical predictions were actually borne out by experimental data covering various physicochemical properties of paraffin hydrocarbons (alkanes).

According to the theory [3], all the alkanes can be separated into groups on the basis of identical structure in branched fragments of hydrocarbon chains. Examples of such groups are listed in the Table. Then, for each (for example n-th) alkane group some physicochemical dimension P (from among the ones listed above) should be a linear function of the number of carbon atoms (n) in the alkane molecule of that group,

$$P_n^{(m)} = 2P_{12} - 3P_{22} + \Delta^{(m)} + P_{22} \cdot n, \qquad (1)$$

with a constant coefficient P_{22}.

Equation (1) can be rewritten in a shorter form,

$$P_{(n)}^{(m)} = \alpha^{(m)} + \beta \cdot n, \qquad (2)$$

where: $\alpha^{(m)}$ = constant for a given group, β = constant for all the groups. In Figs. 1-4 we have shown to what degree is linear dependence (1), (2) of different physicochemical properties fulfilled in each alkane group. It is evident from these figures that the agreement between theory and experiments is completely satisfactory. The values of group constants $\alpha^{(m)}$ were calculated from experimental data and are listed in the Table; in going from group to group we can see a change not only in $\alpha^{(m)}$ (as theoretically expected) but also an insignificant one in β, although theoretically it should remain constant for all the groups. However, these variations in β are

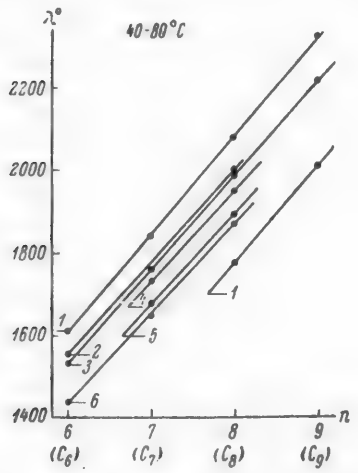

Fig. 2. $\lambda^0 = \frac{L^0}{4.575}$ as a function of the number of carbon atoms in alkane molecules of various groups.
1) n-Alkanes; 2) 3-methylalkanes; 3) 2-methylalkanes; 4) 2,3-dimethylalkanes; 5) 3-ethylalkanes; 6) 2,2-dimethylalkanes; 7) 2,2(n-1)-trimethylalkanes.
Value of λ^0 are in the interval 40-80°.

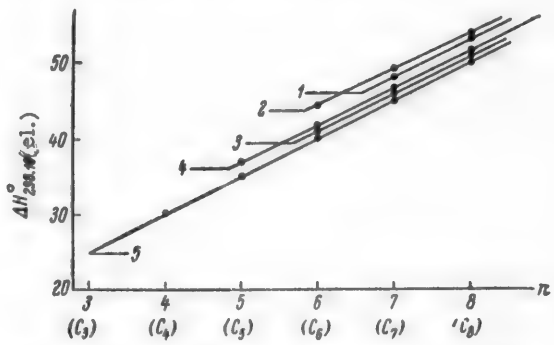

Fig. 3. $\Delta H^0_{(el.)}$ gas at T = 298.16°K as a function of the number (n) of carbon atoms in alkane molecules of various groups.
1) 2,(n-1)-Dimethylalkanes; 2) 2,2-dimethylalkanes; 3) 3-methylalkanes; 4) 2-methylalkanes; 5) n-alkanes.

negligible and its value is very close to constant (as the theory would require).

For such factors as density and boiling point of hydrocarbons in each group we derived [3] equations of the type:

$$d_n^{(m)} = \frac{a^{(m)} + b \cdot n}{g^{(m)} + h \cdot n} \qquad (3)$$

For calculations it is convenient to change it to this form:

$$d_n^{(m)} = A^{(m)} + \frac{B}{n_0^{(m)} + n}, \qquad (4)$$

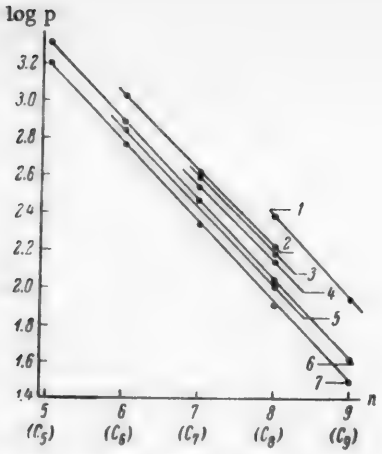

Fig. 4. The logarithm of vapor pressure (at constant temperature 60°) as a function of the number of carbon atoms in alkane molecules of various groups.
1) 2,2,(n-1)-Trimethylalkanes; 2) 2,2-dimethylalkanes; 3) 2,(n-1)-dimethylalkanes; 4) 3,3-dimethylalkanes; 5) 3-methylalkanes; 6) 2-methylalkanes; 7) n-alkanes.

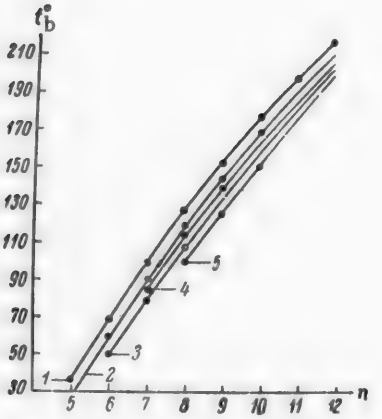

Fig. 6. Boiling point t as a function of the number of carbon atoms (n) in alkane molecules of various groups.
1) n-Alkanes; 2) 2-methylalkanes; 3) 2,2-dimethylalkanes; 4) 3,3-dimethylalkanes; 5) 2,2,(n-1)-trimethylalkanes.

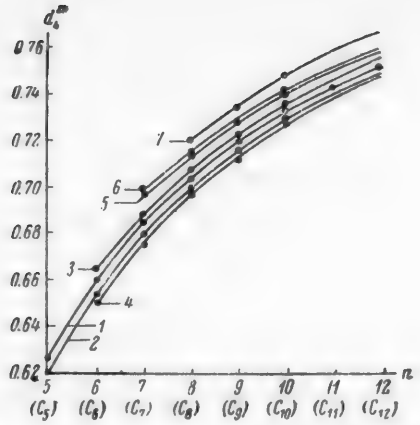

Fig. 5. Density d_4^{20} as a function of the number of carbon atoms in alkane molecules of various groups.
1) n-Alkanes; 2) 2-methylalkanes; 3) 3-methylalkanes; 4) 2,2-dimethylalkanes; 5) 2,3-dimethylalkanes; 6) 6-ethylalkanes; 7) 3,4-dimethylalkanes.

where the new constant $A^{(m)}$, B, $n_0^{(m)}$ can easily be expressed through constants $a^{(m)}$, b, $g^{(m)}$, and n. Similarly, for the boiling point of m-th group hydrocarbons the following equation can be derived:

$$t_n^{(m)} = t_0^{(m)} + \frac{B}{n_0^{(m)} + n} \qquad (5)$$

Comparisons of experimental data on d_4^{20} and t_b (at 760 mm) (for some alkane groups) with results calculated using Formulas (4) and (5) are shown in Figs. 5 and 6. The constants which enter these equations were calculated from experimental data and are listed in the Table.

It is evident from Fig. 4 that Equations (4) and (5) for d_4^{20} and t_b give a satisfactory description of regularities in each alkane group.

The above described regularities can readily be used to calculate physicochemical properties of as yet unstudied hydrocarbons of a given group, if corresponding experimental data is available for other hydrocarbons of the same group; this undoubtedly is of substantial interest in a number of practical cases. For example, we can use the constants from the Table in Formulas (2), (4) and (5) to calculate physicochemical properties of higher hydrocarbons belonging to groups listed in the same Table.

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REACTIONS OF POLYHALOGEN COMPOUNDS WITH ALCOHOLS

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Reactions of carbon tetrachloride with methyl [1] and ethyl [2] alcohols were studied in the previously published papers. These reactions proceed on heating to 200° according to the scheme: $CCl_4 + ROH \rightarrow CHCl_3 + HCl + RC(O)H$. After this, the secondary processes of formation of alkyl chloride and ethers take place. The reaction of carbon tetrachloride with alcohols, with formation of hydrogen chloride proceeds even at lower temperatures under irradiation with ultraviolet light [1], γ-rays [3] and under the influence of an initiator [4].

It appeared interesting to us to determine whether or not these regularities extend to other alcohols and other polyhalogen compounds. With this purpose in mind we studied the thermal reactions of carbon tetrachloride with 1-butanol, 2-butanol, and, on the other hand, the reaction of pentachloroethane and tetrachloroethanes (symmetric and unsymmetric) with methanol.

The reactions of 1-butanol with carbon tetrachloride proceed at a higher temperature (230°) than that with methanol, forming chloroform, hydrogen chloride, water and butyl chloride. However, butyraldehyde could not be detected among the reaction products while butyl butyrate was actually found. Formation of the latter substance may be explained by an ester condensation of butyraldehyde formed in the first stage of the reaction: $2C_3H_8CHO \rightarrow C_3H_8COOC_4H_9$.

Reaction of 2-butanol with carbon tetrachloride proceeds at 210-220° with formation of the expected products: chloroform, hydrogen chloride, methyl ethyl ketones, water and secondary butyl chloride. However, in addition to these substances there were found butylene and a compound with composition $C_5H_8Cl_4$. The structure of the latter was not established. Possibly it was a product of addition of carbon tetrachloride to butylene. The formation of olefins had been noted by us earlier in the reaction of cyclohexanol with carbon tetrachloride. A large amount of cyclohexene was found along with the other products [5].

Thus it was shown that other primary and secondary alcohols react with carbon tetrachloride analogously to the reaction of methyl alcohol.

Then we examined the reactions of pentachloroethane and symmetric and unsymmetric tetrachloroethanes with methyl alcohol.

The radical decomposition of pentachloroethane takes place during irradiation with ultraviolet light and yields hydrogen chloride with dimerization of the resulting radicals [6]. In addition to this there are observed reactions of chlorination of both the pentachloroethane and the resulting derivatives of butane. Hexachloroethane, octachlorobutane, nonachlorobutane and decachlorobutane were isolated.

Hydrogen chloride, formaldehyde, methyl chloride, water, 1,1,2,2-tetrachloroethane and trichloroethylene were isolated after the thermal reaction of pentachloroethane with methanol (210-220°). On the basis of the data obtained one may consider that the process proceeds according to the following equation: $CHCl_2-CCl_3 + CH_3OH \rightarrow CHCl_2-CHCl_2 + CH_2O + HCl$. Formation of trichloroethylene may occur either through cleavage of hydrogen chloride from tetrachloroethane or through the decomposition of the primary radical with evolution of chlorine:

$$CHCl_2-CHCl_2 \rightarrow CHCl=CCl_2 + HCl$$
$$CHCl_2-CCl_2\cdot \rightarrow CHCl=CCl_2 + Cl\cdot$$

The last reaction is analogous to the cleavage of pentachloroethyl radical [7]. The formation of $CHCl_2-\dot{C}Cl_2$ may be regarded as the primary process in the cleavage of chlorine from the CCl_3 group. Thus, the first stage of the process would be the same for CCl_4, C_2Cl_6 and C_2HCl_5.

The difference between the reactions of hexachloroethane and pentachloroethane with methanol consists of the fact that the $C_2Cl_5^{\cdot}$ radical is incapable of cleavage of a hydrogen atom from the alcohol and suffers a total decomposition with evolution of chlorine and formation of perchloroethylene [2]. The $C_2HCl_4^{\cdot}$ radical is able, one one hand, to cleave a hydrogen from the alcohol just like $\dot{C}Cl_3$ radical, and, on the other hand, it can lose chlorine just like $C_2Cl_5^{\cdot}$ radical.

The correctness of the previously made supposition about the absence of the reaction of hydrogen cleavage from the alcohol by the $C_2Cl_5^{\cdot}$ radical has been confirmed by the data in this investigation. If such a reaction did take place, the resulting C_2HCl_5 would have reacted further and should have formed C_2HCl_4 and trichloroethylene. Thus, the reaction with pentachloroethane proceeds by the following scheme:

$$C_2HCl_5 \longrightarrow CHCl_2 - CCl_2 \cdot + Cl \cdot$$
$$Cl \cdot + CH_3OH \longrightarrow HCl + \cdot CH_2OH \text{ or}$$
$$CHCl_2CCl_2 \cdot + CH_3OH \longrightarrow CHCl_2 - CHCl_2 + \cdot CH_2OH$$

In this scheme we presuppose a dissociation at the C–Cl bond in the trichloromethyl group. For a confirmation of this supposition we studied the reaction of methanol with symmetric and unsymmetric tetrachloroethane. This reaction is interesting also from the viewpoint that the symmetric $C_2H_2Cl_4$ is a reaction product of methanol and pentachloroethane.

However, the data obtained by us did not permit us to make any definite conclusions. 1,1,2,2-Tetrachloroethane reacts with methanol at 220-230° with formation of trichloroethylene, water, hydrogen chloride and methyl chloride. Only traces of formaldehyde were detected. This shows that the cleavage of chlorine almost does not occur and the reaction, in the main, proceeds by the scheme:

$$CHCl_2 - CHCl_2 \longrightarrow HCl + CHCl = CCl_2$$
$$CH_3OH + HCl \longrightarrow CH_3Cl + H_2O$$

1,1,1,2-Tetrachloroethane reacts with methanol at 215-220°. In this case water, hydrogen chloride and methyl chloride are formed, along with considerable amounts of tar. Only traces of formaldehyde were detected. Trichloroethylene could not be found. However, the tar containing but 23% of chlorine could form in copolymerization of formaldehyde with halogen compounds.

EXPERIMENTAL

The reaction mixture was sealed into tubes of thick-walled heat resistant glass with length of 60-70 cm and diameter of 12-15 mm. Heating of the tubes was done in tube furnaces until the volume of the resulting aqueous layer ceased to change. The tubes were chilled with a mixture of solid carbon dioxide and toluene prior to being opened. A gas, which was collected in chilled absorption flasks, was evolved in some cases on slow heating of the tubes to room temperature. In experiments with methanol the gas was first passed through water (for absorption of hydrogen chloride and formaldehyde), then through alcoholic ammonia. After cessation of gas evolution the tube with alcoholic ammonia was sealed and heated on a water bath for completion of the formation of the amine salt from methyl chloride and ammonia. Then the mixture was diluted with water and was analyzed for chlorine, from the amount of which there was calculated the yield of methyl chloride. Water through which the gas had been passed did not contain hydrogen chloride or formaldehyde in all the experiments run. The upper aqueous layer was separated after the elimination of gases from the reaction tube. The nonaqueous part was washed with water. Then each layer was analyzed separately. Formaldehyde was determined in the form of dimedone derivative in the aqueous reaction layer as well as in the wash water and after the hydrolysis of the resulting methylal. It was not possible to isolate a sufficient amount of completely pure products in all cases by distillation through a fractionating column (25 theoretical plates) even after repeating the operations several times. Owing to this the elemental analysis in some instances deviated from the theoretical value by 1-2%.

A spectroscopic analysis of some fractions was made following the experiments with 1-butanol and 2-butanol, in addition to the chemical analysis. The spectra of the solutions under study were recorded in the interval from 15 to 4μ on a double beam IKS-2 spectrometer with potassium chloride prism. The thickness of the absorbing layer was 0.1 mm. The identification of the absorption lines which belong to the substance under study was done by comparison of its spectrum with the spectrum of authentically pure substance recorded on the same machine.

1-Butanol–Carbon Tetrachloride. Sixteen g (0.217 mole) of butanol, 16.0 g (0.104 mole) of carbon tetrachloride were heated 20-30 hours at 230°. The evolved gas (0.200 g) was passed into bromine water for determination of butylene. The bromine water was not decolorized. The weight of the aqueous layer was 1.7 g, and that of nonaqueous part was 30.0 g. The aqueous layer and the water from washing the nonaqueous layer contained 0.062 g of hydrogen chloride which was determined by titration. The nonaqueous layer, after washing, weighed 5.7 g less (owing to removal of butanol). After drying with sodium sulfate, the nonaqueous part was distilled through a column with 25 theoretical plate efficiency. A mixture from six reaction tubes was used for this distillation. The first fraction at 60-72° (71.15 g) was examined spectroscopically. Chloroform (λ, 8.2 and 10.9 μ) and primary butyl chloride (λ 7.3, 8.5 μ) and others) were found in it by the method of spectral coincidence. After two redistillations through the fractionating column, a chloroform fraction (61.3-63.0°), with d^0_0 1.5025, $n^{20}D$ 1.440 (qualitative test with resorcinol for chloroform was positive) was isolated from the first fraction. The amount of chloroform determined by heating with aniline, alkali and methanol [8] was 4.28 g calculated for the contents of one reaction tube. The residue after the distillation of the first fraction was distilled at 25 mm vacuum. There was collected the second fraction at 60-75° (1.9 g), d^0_0 0.8937, $n^{20}D$ 1.4113, which consisted of butyl ester of butyric acid (this fraction had the characteristic odor of an ester). The content of butyl butyrate (as determined by saponification of 0.5 N aqueous alcoholic alkali) was 97%. The molecular weight was 138 (calculated 144). The absence of butyraldehyde in the reaction products was proved spectroscopically (by absence of the absorption line of butyraldehyde in the absorption spectra) and by a negative reaction with semicarbazide and 2,4-dinitrophenylhydrazine.

2-Butanol–Carbon Tetrachloride. Sixteen g (0.217 mole) of 2-butanol and 16.0 g (0.104 mole) of carbon tetrachloride were heated 16-20 hours at 210-220°. The butylene generated in the reaction mixture (6.0 g) was transformed into dibromobutane (b.p. 160°, d^0_0 1.8256) by passage into bromine water. The aqueous layer (3.6 ml) and the wash water contained 0.3 g of hydrogen chloride. Four tenths of a gram of methyl ethyl ketone was found in the wash water; 2,4-dinitrophenylhydrazone, m.p. 109° (no depression in mixed melting with authentic sample). The quantitative determination was made by the reaction with hydroxylamine hydrochloride. The nonaqueous part was distilled through the column after washing and drying with sodium sulfate. The mixture from six reaction tubes (114.2 g) was taken for the distillation. There was isolated the following fractions: 1st 58.5-67.0°, 8.6 g; 2nd 67.0-69.0°, 27.0 g; 3rd 69.0-73.0°, 24.1 g; 4th 74-78°, 3.2 g; residue 25.7 g. Three and three tenths grams of butylene was isolated in addition during the distillation. From the first fraction there was isolated 1.6 g of a fraction b.p. 60.7-62.5°, containing chloroform as shown by the qualitative test with resorcinol and by the spectral data. Second and third fractions consisted mainly, as shown by the spectral data, of butyl chloride (λ 7.55, 8.37, 10.30 and 10.67 μ) and a small admixture of chloroform (λ 7.0, 8.20 and 10.9 μ).

By repeated vacuum distillation of the 13.3 g residue at 35 mm vacuum there was isolated 1.7 g of a substance with b.p. 193°, d^0_0 1.338, $n^{20}D$ 1.4820.

Found %: C 30.1; H 4.1; Cl 65.0. M 198. $C_5H_8Cl_4$. Calculated %: C 28.6; H 3.8; Cl 67.7.

Pentachloroethane–Methanol. Thirteen and six tenths g (0.067 mole) of pentachloroethane and 6.4 g (0.200 mole) of methanol were heated 15 hours at 210-220°. There was evolved 3.6 g of a gas (the weight of gas was determined by weight difference of the tube before and after the release of the gases). The aqueous layer (2.4 ml) and the wash water contained 0.030 g of hydrogen chloride and 0.090 g of formaldehyde (m.p. of dimedone derivative 186°, without depression of mixed authentic sample). The mixture from seven tubes was taken for the analysis of the nonaqueous portion. The weight before washing was 131.9 g and after washing 117.6 g. After drying with potassium carbonate the mixture was distilled through the column. There were isolated the fractions: 1st 83.5-96.0°, 4.0 g; 2nd 99.5-125.5°, 3.0 g; 3rd 133.0-140.0°, 3.1 g; 4th 145-147°, 1.0 g; 5th 155-161°, 12.7 g; 6th 161-165.0°, 44.2 g; residue 10 g. Ten grams of methyl chloride was isolated in addition during the distillation. The first fraction contained trichloroethylene, d^{20} 1.441, $n^{17}D$ 1.4720.

Found %: Cl 79.74 . M 128. C_2HCl_3. Calculated %: Cl 80.98. M 131.

The identify of trichloroethylene was proved by the preparation of the organomercury compound $Hg(CCl = CCl_2)_2$ by the reaction with mercuric cyanide.

Found %: Hg 42.9; Cl 45.5. M 445. $C_4Cl_6H_2$. Calculated %: Hg 43.4; Cl 46.2. M 461.

The second fraction was examined for the content of tetrachloroethylene by its reaction with bromine in carbon tetrachloride. No absorption of bromine was observed and a solution of potassium permanganate was not decolorized. The fourth fraction contained 1,1,2,2-tetrachloroethane ($n^{12}D$ 1.491, d_D^{20} 1.590).

Found %: Cl 82.40. M 165. $C_2H_2Cl_4$. Calculated %: Cl 84.52. M 168.

The sixth fraction was unreacted pentachloroethane (d^0_0 1.710, $n^{20}D$ 1.505).

1,1,2,2-Tetrachloroethane–Methanol. Tetrachloroethane (12.8 g; 0.076 mole) and 7.1 g (0.211 mole) of methanol were heated 12-15 hours at 210-215°. No layering of the liquid was observed. Heating for 12 hours at 220-230° did lead to layer formation. There was isolated 0.6 g of methyl chloride. The 2.3 ml, aqueous layer contained 0.004 g of hydrogen chloride while the wash water was neutral. There was found 0.03 g of formaldehyde (dimedone derivative, m.p. 187°). The nonaqueous part was analyzed after combining the contents of six tubes. The weight prior to washing was 100.15 g, and after washing it was 68.4 g. The latter weight was taken for the distillation. There were isolated the fractions: 1st 75.0-100.0°, 2.6 g, containing trichloroethylene (determined by the formation of $Hg(CCl=CCl_2)_2$); 2nd 100.0-139.0°, 2.6 g; 3rd 144.5°, 47.3 g containing unreacted tetrachloroethane (determined by b.p. and index of refraction); residue was 14.0 g.

1,1,1,2-Tetrachloroethane–Methanol. Tetrachloroethane (12.7 g; 0.076 mole) and 7.1 g (0.211 mole) of methanol were heated 12-15 hours at 215-220°. Considerable amount of tar was formed. The evolved gas (4.7 g) contained 1.1 g of methyl chloride. The aqueous layer (1.6 ml) and the wash water contained 0.035 g of hydrogen chloride. Traces of formaldehyde were detected. The nonaqueous part (from eight tubes) gave a stable emulsion on washing with water, this emulsion being broken by steam distillation, followed by drying with potassium carbonate, which gave 143.5 g of product. Distillation gave a fraction of 80-120°, 6.2 g, in which no trichloroethylene was detected (the mercury compound with mercuric cyanide failed to form as it did in previous examples). Neither was there isolated a fraction corresponding to trichloroethane. The weight of the tar after drying at 100° was 0.34 g (from one tube). On heating, the tar evolved hydrogen chloride. The content of chloride in the tar (by sodium fusion) was 23.3%.

SUMMARY

1. The thermal reactions of carbon tetrachloride with 1-butanol and 2-butanol proceed with formation of hydrogen chloride, the appropriate dehydrogenation product of the alcohol (aldehyde or ketone) and chloroform.

2. Dehydrogenation of the alcohol to formaldehyde and formation of hydrogen chloride and tetrachloroethane, which in part loses hydrogen chloride and yields trichloroethylene, was observed after heating pentachloroethane with methanol, as it was with carbon tetrachloride.

3. On heating methanol with symmetric tetrachloroethane there takes place the decomposition of the latter with evolution of hydrogen chloride and trichloroethylene. Dehydrogenation of the alcohol was observed only to an insignificant degree.

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UTILIZATION OF BENZENE AS A SOLVENT IN ACETYLATION REACTION ACCORDING TO FRIEDEL-CRAFTS

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It is evident on examination of the literature data [1-8] about the relative rates of heterolytic reactions in the series of benzene homologs that the reactivity of benzene is considerably lower than that of its alkyl derivatives (Table 1).

It follows from the data shown in Table 1 that the greatest difference in the rates of reaction of alkyl homologs of benzene as compared with benzene itself is observed in bromination, chlorination and chloromethylation; this difference is considerably smaller in reactions of nitration, sulfonation, mercuration and acetylation.

TABLE 1

Relative Rates of Certain Heterolytic Reactions of Monoalkylbenzene C_6H_5-R (for benzene-1)

Reaction	R			
	CH_3	C_2H_5	iso-C_3H_7	tert-C_4H_9
Bromination (Br_2 in CH_3COOH at 25°)	467	354	204	107
Chlorination (Cl_2 in CH_3COOH at 24°)	345	290	176	110
Chloromethylation (CH_2O + HCl in CH_3COOH at 60°)	112	-	—	—
Nitration (HNO_3 in $(CH_3CO)_2O$, HNO_3 + H_2SO_4 at 30°)	23	—	—	15.7
Mercuration ($Hg(OCH_3CO)_2$ in CH_3COOH)	25	—	—	—
Acetylation (CH_3COCl + $AlCl_3$ at 0°)	13.3	—	—	—
(CH_3COCl + $AlCl_3$ at 50°)	8.4	—	—	—
Sulfonation (100% H_2SO_4 in $C_6H_5NO_2$ at 40°)	5.1	—	—	—

The reduction of the relative reaction rate in the series of benzene homologs has the following dependence on the nature of the alkyl substituent: $CH_3 > C_2H_5 >$ iso-$C_3H_7 >$ tert-C_4H_9. The relative reactivity of these homologs of benzene in bromination and chlorination is considerably greater than it is in nitration.

It should be noted that the relative reaction rates in passage from toluene to tert-butylbenzene are decreased, respectively, by 4.35 and 3.14 fold in the reactions of bromination and chlorination, while in nitration the change is but 1.46 fold.

In the reactions of mercuration, acetylation and sulfonation of toluene the reactivity of the latter is of the same order as in the nitration reaction; therefore one should expect that in the above-cited reactions in the series of toluene-tert-butylbenzene there would be observed a regularity that is characteristic of nitration.

Since literature does not cite any comparative data on the reaction of acetylation in the series of alkyl homologs of benzene, it seemed interesting to clarify the possibility of running a selective acetylation of these substances in the presence of benzene in a Friedel-Crafts reaction. This should have a degree of significance for the preparative syntheses of methyl alkylaryl ketones, since the use of benzene as the solvent in this reaction is much more convenient than is the use of the fire-hazardous and toxic carbon disulfide or nitrated hydrocarbons. In addition, here one would find a more complete utilization of alkylated benzene derivatives.

The acetylation was run with acetic anhydride. The following ketones were prepared: acetophenone, p-methylacetophenone, p-ethylacetophenone, p-isopropylacetophenone, p-n-butylacetophenone, p-sec-butylacetophenone, p-tert-butylacetophenone as well as β-methyl-α-acetylnaphthalene.

EXPERIMENTAL

The process of acetylation was run at 10° with the proportion of reactants being 0.5 mole of benzene homolog, 1 mole of benzene, 1 mole of acetic anhydride and 1.2 moles of aluminum chloride. The mixture of hydrocarbon with acetic anhydride was added to the suspension of aluminum chloride in benzene with stirring at such a rate that permitted one to maintain the reaction temperature at 10°. Then the mixture was stirred for one hour at the same temperature, the reaction products were poured into a mixture of ice and concentrated hydrochloric acid, the oily layer was separated, washed with water, aqueous solution of sodium carbonate, then again with water, dried over anhydrous calcium chloride and distilled in vacuum.*

TABLE 2

Properties of Products of Acetylation of Alkyl Homologs of Benzene p-$RC_6H_4COCH_3$ and the Melting Points of Their 2,4-Dinitrophenylhydrazones

R	B.p. (pressure in mm)	Yield (in %)	Melting points of 2,4-dinitrophenylhydrazones	
			found	literature data
H	95° (20)	6.7	249—250°	249° [9]
CH_3	120 (20)	85.0	258—259	260 [10]
C_2H_5 . . .	86 (3)	74.0	209	208—209 [11]
iso-C_3H_7	100 (3)	70.0	185	185—186 [11]
n-C_4H_9 . .	112 (3)	65.0	160	160 [12]
sec.-C_4H_9	122 (3—4)	62.0	145—147	145—146 [11]
tert.-C_4H_9	135 (20)	60.0	212	212.5—213.5 [11]

The yields of the ketones prepared by the above method, as well as some of their physicochemical properties and the melting points of the corresponding 2,4-dinitrophenylhydrazones are shown in Table 2.

It is interesting to note that practically no formation of ortho- or meta-isomers was detected under the selected conditions of acetylation.

* The content of the ketone in the reaction mixture was determined in parallel by oximation.

Besides the indicated ketones there was obtained β-methyl-α-acetylnaphthalene by acetylation, under the same conditions, of β-methylnaphthalene in yield of 67% of theoretical. The product was an oil with b.p. 168-169° at 3 mm, n^{24}_D 1.6206, which was not identified any further. Simultaneously with the β-methyl-α-acetylnaphthalene there was obtained acetophenone (from the benzene used as the solvent) in a yield of about 20% of theoretical.

SUMMARY

1. It was shown that in acetylation according to Friedel-Crafts of benzene and a series of its homologs, the reactivity of the latter exceeds considerably the reactivity of benzene itself.

2. The difference in reactivity of benzene and its alkyl homologs permits the use of benzene as the solvent for acetylation according to Friedel-Crafts method.

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ACCELERATING EFFECT OF AMINES ON ISOTOPE EXCHANGE OF SULFUR IN ORGANIC POLYSULFIDES

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It is known that some amines show an accelerating action on chemical reactions with participation of elemental sulfur and organic polysulfides. There are literature data on acceleration of the process of addition of sulfur to diethyl disulfide in the presence of dibutylamine [1, 2]. There is information to the effect that diethylamine accelerates the addition of sulfur to cyclohexene [3], and that some amines aid the transition of polymeric sulfur into the soluble state [4, 5]. The accelerating effect [6-8] of amines on the process of sulfur vulcanization of rubber is also known. In one of our studies [9] there had been observed the accelerating action of dibutylamine on the isotope exchange of sulfur between diethyl trisulfide and elemental sulfur, as well as on the exchange of RS groups in polysulfides. However, a more systematic examination of the problem of the effect of composition and structure of the amines on their catalytic activity in the reactions in which sulfur participates was not made at that time.

One may take any of the above listed systems, for example the reaction of addition of sulfur to disulfide RS–SR with formation of RS–S–SR and other polysulfides, a reaction that had been studied in some detail [2] in cases of addition of sulfur to diethyl disulfide in the presence of dibutylamine, for the study of comparative activity of amines differing in composition and structure. However, it is quite difficult, and sometimes impossible, to run a quantitative analysis of such systems containing a mixture of products with similar constants.

We attempted in this work to carry out a comparison of activity of various amines by the way of study of the reaction of isotope exchange of sulfur between organic polysulfides and elemental sulfur. Apparently the mechanism of the activating action of the amines on sulfur and polysulfides in the systems examined above is the same and therefore the reaction of isotope exchange of sulfur may be regarded as being a model reaction.

Exchange ability of sulfur in organic polysulfides depends to a great extent on the composition and the structure of the radicals R and on the number of sulfur atoms in the polysulfide bridge [9]. The polysulfides with aliphatic radicals possess stronger polysulfide bonds and are less susceptible to exchange than are polysulfides with aromatic radicals. Introduction of a methylene group between the phenyl ring and the polysulfide bridge leads to the phenomenon in which the exchange of sulfur, for example in dibenzyl trisulfide $C_6H_5CH_2-S-S-S-CH_2-C_6H_5$ proceeds under conditions which are close to those needed for sulfur exchange in polysulfides with aliphatic radicals. The exchange ability rises with increased number of atoms of sulfur in the polysulfide.

For making this study we took polysulfides in which the sulfur exchange takes place under relatively drastic conditions: dibenzyl trisulfide and diethyl trisulfide.

It had been shown earlier [10] that only the middle atom of sulfur is the exchangeable sulfur atom in these polysulfides.

$$RS-S-SR + \overset{*}{S} \rightarrow RS-\overset{*}{S}-SR + S$$

Addition of certain amines brings about a considerable change in the conditions for sulfur exchange in these compounds, which fact permitted us to compare the activities of various amines.

It should be noted that such reactions of exchange are accompanied by addition of sulfur and by formation of higher polysulfides. The analysis of a mixture of polysulfides is as complicated a matter as in the reactions

cited above. However, it is possible to secure quite single-valued data on the rate of the progress of the reaction by analyzing the activity of elemental sulfur. Alteration of activity of sulfur may take place only as the result of exchange with the middle sulfur atom of the polysulfide. Considering that the exchangeability of polysulfides, which are richer in sulfur, in much greater, the addition of active sulfur will change only the amount of residual free sulfur and will not affect its activity. The decompositions of the trisulfides with evolution of sulfur do not take place under the experimental conditions used by us. The correctness of these hypotheses was checked by us experimentally by making a balance sheet of radioactivity. We used the radioactive isotope of sulfur S^{35} for the labelled atom.

Experiments with isotope exchange were run in sealed ampoules in toluene in nitrogen atmosphere. The concentration of solutions was 0.28 moles per liter of trisulfide and 0.28 gram-atoms per liter of radioactive sulfur. All exchange accelerators were taken in the amount equal to 5% of the trisulfide weight. The separation of the components after the exchange was done as follows. The solvent was evaporated in the cold (by means of a nitrogen flow) and the residual mass was treated with acetone; here the trisulfide, the higher polysulfides and also amines went into solution, while sulfur remained mainly undissolved. After 2- or 3-fold washing with acetone, the sulfur was recrystallized from benzene and a known sample (about 0.01 g) was oxidized by the Carius method and was precipitated with benzidine hydrochloride. The activity of the precipitates of benzidine sulfate was determined. In some of the experiments the trisulfide was isolated from the mixture for a control: in case of dibenzyl trisulfide this was done by fractional crystallization from alcohol, while in the case of diethyl trisulfide it was separated by vacuum fractionation; the activity of sulfur in these compounds after the exchange was then determined. Part of the specimens used in the work: dibenzyl trisulfide, diethyl trisulfide, sodium diisobutyldithiocarbamate, piperidine cyclopentamethylenedithiocarbamate, were synthesized by us, while the remaining specimens were taken in ready state. All these substances were additionally purified and had characteristics which corresponded to the literature data.

The results of experiments with sulfur exchange between dibenzyl trisulfide and elemental sulfur, as well as between diethyl trisulfide and elemental sulfur in the absence of accelerators are given in Table 1.

TABLE 1

Temp.	Time (hours)	Activity of sulfur (cts./min) before exchange	Activity of sulfur (cts./min) after exchange	Percentage of exchange
	Dibenzyl trisulfide – sulfur			
80°	1	2610	2600	0
100	1	1900	1900	0
100	2	2608	2610	0
120	1	2610	2505	4
120	2	2730	2510	16
140	1	1900	1450	15
200	1	1900	908	100
	Diethyl trisulfide – sulfur			
75	2	2360	2370	0
90	2	2360	2360	0
100	2	2180	2170	0
125	2	2180	1930	23

It is evident that sulfur exchange in the trisulfides studied by us begins in the absence of accelerators only at 120°. Considering the data shown in Table 1 we selected the time interval of two hours as the standard. The analysis of the products after exchange was run in all experiments two hours after the beginning of the reaction.

The results of experiments with sulfur exchange between dibenzyl trisulfide and radioactive sulfur in the presence of various amines are shown in Table 2. Analogous data for the diethyl trisulfide are given in Table 3. The names and the formulas of the amines used by us and the percentage of exchange at the indicated temperatures are shown in the tables.

TABLE 2

Dibenzyl Trisulfide–Sulfur

No.	Exchange accelerator		Percentage of exchange			
	name	formula	25°	41°	75°	125°
1	Without accelerator	—	0	0	0	16
2	n-Propylamine	$C_3H_7NH_2$	77	100	—	—
3	Isobutylamine	$(CH_3)_2CHCH_2NH_2$	—	66	100	—
4	n-Amylamine	$C_5H_{11}NH_2$	43	62	86	—
5	n-Heptylamine	$C_7H_{15}NH_2$	27	41	70	—
6	Aniline	$C_6H_5NH_2$	0	0	0	12
7	Diethylamine	$(C_2H_5)_2NH$	—	64	—	—
8	Di-n-propylamine	$(C_3H_7)_2NH$	—	88	—	—
9	Di-n-butylamine	$(C_4H_9)_2NH$	90	100	—	—
10	Di-n-amylamine	$(C_5H_{11})_2NH$	74	100	—	—
11	Dibenzylamine	$(C_6H_5CH_2)_2NH$	0	0	7	80
12	Diphenylamine	$(C_6H_5)_2NH$	0	0	0	16
13	Tri-n-butylamine	$(C_4H_9)_3N$	0	0	43	90
14	Triisobutylamine	$(C_4H_9)_3N$	0	0	35	88
15	Tri-n-amylamine	$(C_5H_{11})_3N$	0	0	0	72
16	Tribenzylamine	$(C_6H_5CH_2)_3N$	0	0	0	16
17	Dimethylaniline	$C_6H_5(CH_3)_2N$	0	0	0	14
18	2-Mercaptobenzothiazole		0	0	0	14
19	Tetramethylthiuram disulfide	$(CH_3)_2N-CS-S-S-CSN(CH_3)_2$	0	0	0	37
20	Sodium diisobutyldithiocarbamate	$(C_4H_9)_2N-CS-SNa$	—	—	92	100
21	Piperidine cyclopentamethylenedithiocarbamate	$C_5H_{10}N-CS-SH \cdot HNC_5H_{10}$	—	85	100	—

TABLE 3

Diethyl Trisulfide–Sulfur

No.	Exchange accelerator		Percentage of exchange			
	name	formula	25°	41°	75°	125°
1	Without accelerator	—	0	0	0	23
2	Isobutylamine	$(CH_3)_2CHCH_2NH_2$	61	100	—	—
3	Aniline	$C_6H_5NH_2$	0	0	0	26
4	Di-n-butylamine	$(C_4H_9)_2NH$	—	90	100	—
5	Dibenzylamine	$(C_6H_5CH_2)_2NH$	0	21	—	92
6	Tri-n-butylamine	$(C_4H_9)_3N$	—	—	33	94
7	Tetramethylthiuram disulfide	$(CH_3)_2N-CS-S-S-CS-N(CH_3)_2$	0	0	0	43
8	Sodium diisobutyldithiocarbamate	$(C_4H_9)_2N-CS-SNa$	54	75	—	—
9	Piperidine cyclopentamethylenedithiocarbamate	$C_5H_{10}N-CS-SH \cdot HNC_5H_{10}$	92	100	—	—
10	p-Nitroaniline	$NO_2C_6H_4NH_2$	0	0	0	5
11	Diphenylguanidine	$(C_6H_5NH)_2C=NH$	40	77	96	100
12	Monoethanolamine	$NH_2CH_2CH_2OH$	0	0	25	75
13	Diethanolamine	$NH(CH_2CH_2OH)_2$	0	30	64	100
14	Triethanolamine	$N(CH_2CH_2OH)_3$	0	0	15	70

It is evident from comparison of data in Tables 1-3 that the catalytic activity of various amines depends considerably on their composition and structure.

In the series of simple amines (compounds 2-17 in Table 2 and 2-6 in Table 3) the primary and the secondary amines with aliphatic radicals are most active. Addition of a small amount (about 5%) of such amines to the

system makes the latter exchangeable even at room temperature while in the absence of the amines the exchange takes place only with difficulty at 125°.

Among primary amines the dependence of catalytic activity on the radical length is clearly displayed: the longer the aliphatic chain the less active is the amine. The amines studied by us (substances 2-5 in Table 2) may be arranged according to the accelerating action in the following series: $C_3H_7NH_2$ > $C_4H_9NH_2$ > $C_5H_{11}NH_2$ > > $C_7H_{15}NH_2$. Among secondary amines (substances 7-10 in Table 2) no such regularity is observed.

Tertiary amines with aliphatic radicals (substances 13-15 in Table 2) are considerably less active than are the primary and the secondary amines. The accelerating effect of these amines is shown only at a temperature about 70°.

Aromatic amines, such as primary ones – aniline (substance 6 in Table 2 and substance 3 in Table 3), as well as secondary ones – diphenylamine (substance 12 in Table 2) as tertiary ones – dimethylaniline (substance 17 in Table 3) do not accelerate the exchange at all. The sulfur exchange proceeds in their presence just as its does in the pure system: at 125° the extent is 12-16%.

As to benzylamines, they occupy an intermediate position between the corresponding aliphatic and aromatic amines. Dibenzylamine (substance 11 in Table 2 and substance 5 in Table 3) is considerably less active than are aliphatic secondary amines and more active than diphenylamine. Just as with the aliphatic compounds, the secondary amine – dibenzylamine – is more active than tertiary tribenzylamine.

Rather interesting was the fact that such ultraaccelerators of rubber vulcanization as sodium diisobutyldithiocarbamate (substance 20 in Table 2 and substance 8 in Table 3) and piperidine cyclopentamethylenedithiocarbamate (substance 21 in Table 2 and substance 9 in Table 3) are active accelerators of sulfur isotope exchange. Evidently the elemental acts of the reactions between the accelerators and sulfur, which lead to rubber vulcanization on one hand and to isotope exchange on the other hand, are one and the same, whereby the parallelism is quite natural.

The high temperature vulcanization accelerators: mercaptobenzothiazole (substance 18 in Table 2), thiuran (substance 19 in Table 2 and substance 7 in Table 3) practically do not accelerate the exchange under the conditions of the experiments at 120° or below. However, at 125° thiuram turned out to be more active than mercaptobenzothiazole. This fact agrees well with the data on isotope exchange of sulfur in these compounds: thiuram begins to exchange with elemental sulfur at a noticeable rate at 110° while mercaptobenzothiazole reacts with sulfur at a higher temperature (about 130-135°).

Diphenylguanidine (substance 11 in Table 3) is close in its properties to primary and secondary aliphatic amines and is a very active accelerator of exchange.

Mono- and di-ethanolamines (substances 12 and 13 in Table 3) are considerably less active than the simple primary and secondary amines with aliphatic radicals. Triethanolamine has the same activity as tertiary amines with aliphatic radicals.

It was interesting to follow up the change of activity of aromatic amines after introduction of polar substituents into the aromatic ring. We examined the accelerating activity of p-nitroaniline (substance 10 in Table 3). It turned out that this amine, just as aniline, completely fails to accelerate the exchange reaction.

It should be noted that the results obtained in this work relative to the great difference in activity of amines with aliphatic and aromatic radicals are in complete agreement with the data in a series of publications [2, 11] on the study of the reaction of addition of sulfur to diethyl disulfide in the presence of amines.

While in paper [2] there was observed a considerable activating effect of an aliphatic amine – dibutylamine – on the reaction of addition of sulfur to diethyl disulfide, it was found in paper [11] that aromatic amines – aniline and dimethylaniline – do not accelerate this reaction at all.

An analogous observation about the decrease of activity of amines after introduction of aromatic radicals into them was made in paper [12] in a study of vulcanizing activity of benzothiazolesulfenamides. The authors found that the accelerating reaction of these compounds depends on the nature of the substituent in the amino group. Introduction of aromatic radicals sharply lowers the activity of these compounds as vulcanization accelerators.

The problem of the mechanism of the accelerating action of amines on reactions in which polysulfides and elemental sulfur take part has been partially examined in the literature [1, 4, 5]. Some considerations have been expressed. Thus, Weslake and co-workers [1] observing the activating action of dibutylamine on the reaction of addition of sulfur to diethyl disulfide expressed the supposition that the amine weakens the S–S bond in the disulfide and thus aids the addition of sulfur. They also did not exclude the possibility of formation of RS radicals under the influence of the amine, followed by the addition of sulfur to these radicals.

According to Krebs' concepts [4, 5] amine in passing into the ammonium state ruptures the S–S bonds of sulfur, forming peculiar aminopolysulfides with an ionogenic termination, with the type $R_3N^+-S-S-S-S-S-S-S-S^-$. Such a complex may realize several acts of addition of sulfur and the rate of the process may be sufficiently great.

However, such schemes are purely imaginary, are not confirmed by any experimental facts, and have been expressed on the basis of isolated individual observations.

From analysis of the results shown in Tables 2 and 3 one may conclude that Krebs' scheme cannot be accepted for the basis of an explanation of the observed regularities. Actually, if the basic factor in the accelerating effect of amines is the transition into the ammonium state, one should expect that tertiary amines, which form quaternary ammonium compounds most readily, should not be less active than primary and secondary amines. It was established experimentally that tertiary amines are considerably less active. In addition, it is known that aromatic amines are also capable of forming ammonium compounds and, according to Krebs' scheme they ought to be active accelerators. But as shown by the experimental data, aromatic amines are completely inactive in these processes up to 125°. The circumstance that among amines the most active are those compounds with aliphatic radicals which have an unsubstituted hydrogen atom in the amino group calls for some attention. Evidently a mobile hydrogen atom in the amine plays a rather important role in these processes. Evidently the low activity of aromatic amines, in comparison with the aliphatic ones, is caused by the different mobility of hydrogen atoms in them.

We attempted to obtain some data on the character of complexes formed by amines with sulfur and polysulfides, through the experimental route.

If the basis for the accelerating action of amines is the formation of ammonium compounds of the type such as $R_3N^+-S-S-S-S-S^-$, then one may hope to discover such complexes by measurement of the dipole moments. We measured the dipole moment of dibutylamine in benzene in the presence of sulfur at 25°, as well as the dipole moment of equimolar mixture of an amine and sulfur maintained at 100° for ten hours. No material changes of polar properties of these solutions were observed by us in comparison with the additive magnitude. Values close to additive ones were also obtained in the measurement of dipole moment of equimolar mixture of dibutylamine and diethyl trisulfide. In the calculation for the complex $(C_4H_9)_2NH \cdot (C_2H_5)_2S_3$ there were obtained the following results: 2.3 D for a mixture maintained at 25°, and 2.4 D for a mixture heated at 100° for five hours. The additive scheme in a parallel distribution of the dipoles of dibutylamine (1.03 D) and diethyl trisulfide (1.64 D) gives the maximum value of 2.67 D for the complex, i.e., one that is close to the experimental result. Consequently, the formation of any notable amounts of polar complexes in the systems under study was not observed.

The cited material, both purely chemical and physicochemical, seems to us to be completely adequate for the conclusion that the accelerating action of amines is not connected with their transition into the ammonium state. Evidently the reaction of amines with sulfur and polysulfides has a homolytic rather than heterolytic character.

We attempted to use diphenylpicrylhydrazyl (DFPG) as an indicator for the radicals in the systems under study. Solutions of sulfur and diethyl trisulfide in benzene do not decolorize the diphenylpicrylhydrazyl (0.001 N) at 25° for a very long time (over 4 days). Dibutylamine in benzene reacts slowly with DFPG. Addition to the dibutylamine solution of a solution of sulfur or diethyl trisulfide considerably (more than twice) accelerates the reaction with DFPG. These, thus far purely qualitative, results permit us to make the preliminary conclusion about the radical mechanism of the accelerating action of amines.

Clarification of the nature of the reaction of amines with sulfur, as well as with organic polysulfides, inorganic polysulfides and other sulfur-bearing compounds, has a considerable interest, since these reactions lie in the foundation of such most important technological processes as rubber vulcanization, preparation of sulfur dyes, etc. This problem, as may be seen from the above, remains unclarified to this day.

Rather valuable data on the character of the reaction of amines with sulfur and polysulfides may be evidently obtained by a study of the vibrational and electronic spectra of these systems. Work in this direction will be continued in the future.

SUMMARY

1. The effect of composition and structure of amines on the acceleration of the reaction of isotopes exchange of sulfur between dibenzyl trisulfide and radioactive sulfur (elemental), as well as between diethyl trisulfide and elemental sulfur, were studied. The accelerating action of 26 different compounds on this exchange was investigated, among these compounds being a series of industrial rubber vulcanization accelerators.

2. It was shown that ultra-accelerators of rubber vulcanization – piperidine cyclopentamethylenedithiocarbamate and sodium diisobutyldithiocarbamate – are active exchange accelerators. High temperature vulcanization accelerators – mercaptobenzothiazole and thiuram – practically do not accelerate the exchange under the experimental conditions used (120°).

3. The polar properties (dipole moments were measured) of s number of systems under study were explored and some conclusions were made as to the mechanism of the reaction of amines with sulfur and polysulfides.

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SYNTHESIS OF 2-ETHYLANTHRONE AND 2-ETHYL-10-OXANTHRONE LABELED WITH CARBON C^{14} IN THE NUCLEUS AND A STUDY OF SOME OF THEIR PROPERTIES

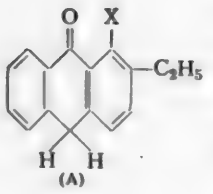
S. V. Siavtsillo, V. I. Savushkina and E. M. Zhernovskaia

2-Ethylanthrone, labeled with carbon C^{14} in the nucleus was synthesized by reduction of 2-ethylanthraquinone labelled with carbon C^{14} [1]. The reduction was run analogously to that of anthrone [2]. 2-Ethylanthrone was obtained in the pure state (m.p. 62°) and did not contain the enolic form; it did not tautomerize after prolonged standing in the solid state or in benzene solutions. Previously [3] 2-ethylanthrone had been obtained only in a mixture with 2-ethylanthranol by solution of 4-ethyldiphenylmethanecarboxylic acid in concentrated sulfuric acid. The product had m.p. 67-75°.

From 2-ethylanthrone labeled with carbon C^{14} there was prepared the previously undescribed 2-ethyl-10-oxanthrone (m.p. 92-3°) by the scheme used by Meyer [4] in the synthesis of oxanthrone, i.e., by the way of bromination of 2-ethylanthrone with a subsequent hydrolysis of 2-ethyl-10-bromoanthrone labeled with carbon C^{14}. In order to avoid the formation of products of oxidation, the bromination of 2-ethylanthrone and isolation of 2-ethyl-10-bromoanthrone were run at a low (from −8° to −20°) temperature.

For hydrolysis of 2-ethyl-10-bromoanthrone there was used a more concentrated (75%) aqueous solution of acetone and the recrystallization of 2-ethyl-10-oxanthrone was done from a mixture of solvents taken in definite proportion. 2-Ethyl-10-oxanthrone is stable in the solid state and tautomerizes on standing in benzene, alcoholic and alkaline solutions.

EXPERIMENTAL



(A)

2-Ethylanthrone. (A). Into a round bottom flask with a reflux condenser, a thermometer and a dropping funnel there was charged a mixture consisting of 13 g (110 millimoles) of granulated tin, 11.2 g (47 millimoles) of 2-ethylanthraquinone (activity 33 μ Cu) and 80 ml of glacial acetic acid. The flask contents were heated to 120-130° and into the boiling mixture there was added 42 g of hydrochloric acid (d 1.17) over a one hour period. The mixture was kept at this temperature for half an hour, the hot solution being then filtered through a funnel with a porous glass plate.

Three hundred ml of water was added to the filtrate; the oily lower layer which separated was extracted with ether, the ethereal solution being then washed with water to a neutral reaction and was then dried with freshly roasted sodium sulfate. Crystalline 2-ethylanthrone was isolated on mixing the ethereal solution with petroleum ether, both precooled with solid carbon dioxide. The precipitate was filtered off through a chilled (with solid carbon dioxide) filter with a porous glass plate, and was washed with petroleum ether, after which it was dried in a vacuum desiccator. After a second crystallization there was obtained 5.6 g of 2-ethylanthrone in the form of white needles with m.p. 60-62°.

The yield based on radioactivity in the original 2-ethylanthraquinone was 49%. The determination of activity has been described before [5].

Found %: C 86.39; H 6.40. $C_{16}H_{14}O$. Calculated %: C 86.50; H 6.30.

Ultraviolet absorption spectra of 0.001 molar solution of the substance in carbon tetrachloride and of anthrone (m.p. 152° [2]) were taken for the identification of the compound synthesized by us; the SF-4 spectrophotometer was used.*

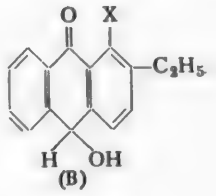
The compound prepared by us had a spectrum that was identical with that of anthrone in the region from 3500 to 2500 A; this confirms the fact that the compound is 2-ethylanthrone and not 2-ethylanthranol.

2-Ethylanthrone did not change on standing in air for several months in the solid state or in benzene solutions. It is readily soluble in benzene without fluorescence, in methyl alcohol with blue fluorescence, and is noticeably soluble in 5% aqueous solution of sodium hydroxide with bright green fluorescence. The latter phenomenon is explained by the fact that 2-ethylanthrone, in contrast with anthrone [6], suffers a tautomeric transformation into 2-ethylanthranol, which rapidly oxidized to 2-ethylanthraquinone, even at room temperature in aqueous alkaline solution.

2-Ethylanthranyl Acetate. 2-Ethylanthrone (1 g) was refluxed in a flask with a reflux condenser with 1 ml of glacial acetic acid and 7 ml of pyridine for two hours in a stream of carbon dioxide. Diluted with water the resulting solution gave an oil which solidified on cooling. After recrystallization from a mixture of ethyl and petroleum ethers there was obtained a lemon yellow precipitate with m.p. 90-92°.

Found %: C 81.37; H 6.31. $C_{18}H_{16}O_2$. Calculated %: C 81.80; H 6.06.

2-Ethyl-10-oxanthrone (B). To a solution of 2-ethylanthrone (2 g, activity 24.2 μ Cu) in carbon disulfide (100 ml) there was added 0.65 ml of bromine dropwise over forty minutes, at first at −8°, then at −15° to −20°. The resulting solution was filtered from the precipitated tarry material. The precipitate of 2-ethyl-10-bromoanthrone, which formed after the solution had been chilled with dry ice to −50° to −60°, was filtered through a funnel with a porous glass plate, chilled with dry ice, and the product was washed with chilled petroleum ether. M.p. 90-91°. Yield: 78%.



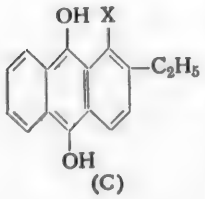
(B)

Found %: Br 26.13. $C_{16}H_{13}OBr$. Calculated %: Br 26.55.

The resulting 2-ethyl-10-bromoanthrone (2.3 g) was gradually heated with stirring at reflux in 75% solution of acetone (120 ml) until it dissolved completely. After dilution of the solution with ten volumes of water followed by standing for 2-3 hours, there formed a precipitate with light yellow color, which was filtered off, washed with water and dried in a vacuum desiccator. The resulting compound (1.52 g) with m.p. 88-90° was 2-ethyl-10-oxanthrone with admixture of 2-ethylanthraquinone. After recrystallization from a mixture of benzene (20 ml) and petroleum ether (60 ml) chilled to −10°, there was obtained 1.3 g of 2-ethyl-10-oxanthrone with m.p. 92-93°. The yield based on radioactivity of initial 2-ethylanthrone was 59%.

Found %: C 80.53; H 6.16. $C_{16}H_{14}O_2$. Calculated %: C 80.65; H 5.92.

2-Ethyl-10-oxanthrone forms white needles; it does not change on standing for five months in air. It is readily soluble in benzene, alcohol and ether and is insoluble in petroleum ether. It isomerized gradually to 2-ethylanthrahydroquinone (C), which oxidized in air to 2-ethylanthraquinone, in solutions in benzene and methyl alcohol at room temperature.



(C)

An analogous isomerization of 2-ethyl-10-oxanthrone was observed on heating in 5% aqueous solution of alkali, when an intense red coloration of the solution appeared. On oxidation of the alkaline solution there was isolated some 2-ethylanthraquinone.

2-Ethyl-10-oxanthrone standing in benzene solution over Raney nickel catalyst in nitrogen atmosphere at 20° isomerized in 180 hours to the extent of about 50% into 2-ethylanthrahydroquinone, while at 60° this reaction proceeded completely in the course of six hours.

Hydrogenation of 2-ethylanthrone and 2-ethyl-10-oxanthrone. On hydrogenation of 2-ethylanthrone (5 g) in benzene solution (50 ml) in the presence of Raney nickel at

*The work was done by K. K. Popkov.

60° over 20 hours there was observed the absorption of hydrogen and formation of a red oil. After repeated fractional crystallization from various solvents there was isolated 2-ethylanthraquinone with m.p. 104-106° and 2-ethylanthracene with m.p. 155-156°. The formation of 2-ethylanthraquinone can be evidently explained by isomerization of 2-ethylanthrone into 2-ethylanthranol, in the process of hydrogenation, with subsequent oxidation of the latter in air to 2-ethylanthraquinone.

On hydrogenation of 2-ethyl-10-oxanthrone (1 g) in benzene (25 ml) under the same conditions there occurs the formation of 2-ethylanthrone (m.p. 60-62°), 2,2'-diethyl-10,10'-dihydrodianthrone (m.p. 190-192°), 2-ethylanthracene (m.p. 155-156°), 2-ethylanthraquinone (m.p. 104-106°) and 1,2,3,4-tetrahydro-2-ethylanthraquinone (m.p. 165-166°).

Oxidation of 2-ethylanthrone and 2-ethyl-10-oxanthrone. In oxidation of 2-ethylanthrone in benzene solution at 60° over six hours by atomic oxygen formed in the decomposition of hydrogen peroxide in the presence of Raney nickel, there is formed mainly 2,2'-diethyl-10,10'-dihydrodianthrone and an insignificant amount of 2-ethylanthraquinone.

In oxidation of 2-ethyl-10-oxanthrone with atomic oxygen in benzene solution at room temperature and at 60°, no noticeable uptake of oxygen was observed. The appearance of an insignificant amount of 2-ethylanthraquinone in this case can be explained by isomerization of 2-ethyl-10-oxanthrone.

SUMMARY

1. 2-Ethylanthrone was synthesized and isolated for the first time in a form labeled with carbon C^{14}; the yield was 51%. There was prepared the acetate of 2-ethylanthranol (m.p. 90-92°).

2. There was synthesized the previously undescribed 2-ethyl-10-oxanthrone, labeled with carbon C^{14} in the nucleus, in 59% yield.

3. The reactions of hydrogenation and oxidation of the indicated compounds were studied.

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TETRAACYLOXYSILANES IN ORGANIC SYNTHESIS

XVI. BENZOYLOXYTRICHLOROSILANE AND REACTIVITY OF BENZOYLOXY GROUP

Iu. K. Iur'ev and Z. V. Beliakova

An attempt to prepare acetoxytrichlorosilane by the action of an excess of silicon tetrachloride on acetic acid failed to give the desired reult, as reported by Goubeau and Mundiel [1], and the sole product of this reaction was tetraacetoxysilane; acetoxytrichlorosilane was prepared only by the action of silicon tetrachloride on sodium acetate. As to benzoyloxytrichlorosilane, this substance has not been prepared as yet.

In a series of studies on acylation of compounds of aromatic nature by means of tetraacetoxysilanes we prepared the latter by reaction of organic acids with silicon tetrachloride in a suitable solvent (benzene, nitrobenzene, carbon disulfide).

In a more detailed study of the reaction between silicon tetrachloride and benzoic acid we discovered that during the action of an excess of silicon tetrachloride on benzoic acid (molar ratios 1.7 : 1 and 2 : 1) in the absence of a solvent and with heating of the reaction mixture for twelve hours with a subsequent distillation of the reaction product in vacuum, there is formed a nearly quantitative yield of benzoyloxytrichlorosilane (I):

$$C_6H_5COOH + SiCl_4 \longrightarrow C_6H_4COOSiCl_3 + HCl \qquad (I)$$

According to the data provided by Rauter [2] and Montonna [3] organic acids react with excess silicon tetrachloride on being heated in closed vessels to 150-160°, forming the corresponding chlorides of the acids and silica gel (II):

$$SiCl_4 + 4RCOOH \longrightarrow 4RCOCl + [Si(OH)_4] \qquad (II)$$

The industrial method of preparation of benzoyl chloride from benzoic acid and silicon tetrachloride [4] is based on this reaction. It was supposed that the reaction proceeds through the stage of formation of tetraacyloxysilane (III) which under the further action of excess silicon tetrachloride yields the acyl chloride and silicon dioxide (IV):

$$4RCOOH + SiCl_4 \longrightarrow Si(OCOR)_4 + 4HCl \qquad (III)$$

$$Si(OCOR)_4 + SiCl_4 \longrightarrow 4RCOCl + 2SiO_2 \qquad (IV)$$

However, the data obtained by us indicate without a doubt that a reaction of this type proceeds by a more complex route.

Thus, by treating benzoic acid with excess silicon tetrachloride for five hours (the reagent proportion and the conditions of the reaction being exactly correspondent to those indicated in the paper by K. A. Andrianov) we then distilled the unreacted silicon tetrachloride on a steam bath and, having distilled the residue in vacuum, obtained a 36% yield of benzoyloxytrichlorosilane.

After heating benzoic acid with excess silicon tetrachloride for 4-5 hours and standing for 12 hours at room temperature there are separated some crystals of tetrabenzoyloxysilane.

On heating tetrabenzoyloxysilane on a water bath with excess silicon tetrachloride and distillation of the reaction product in vacuum, there is obtained a 53.5% yield of benzoyloxytrichlorosilane.

Benzoyloxytrichlorosilane is a colorless liquid which fumes in air and distills in vacuum with slight decomposition, analogously to acetoxytrichlorosilane, which is decomposed partially on being distilled in vacuum [1].

Distillation of benzoyloxytrichlorosilane at atmospheric pressure leads to its thermal decomposition into benzoyl chloride, silicon tetrachloride and silicon dioxide (V):

$$2C_6H_5COOSiCl_3 \longrightarrow 2C_6H_5COCl + SiCl_4 + SiO_2 \qquad (V)$$

Distillation of a mixture of benzoyloxytrichlorosilane and tetrabenzoyloxysilane taken in the proportion required by the following equation also leads to formation of benzoyl chloride in 63% yield (VI):

$$2C_6H_5COOSiCl_3 + Si(OCOC_6H_5)_4 \longrightarrow 6C_6H_5COCl + 3SiO_2 \qquad (VI)$$

The formation of benzoyl chloride should be represented not by Equation (IV) but by Equations (V) and (VI) as the result of reaction of benzoyloxytrichlorosilane and tetrabenzoyloxysilane (VI) which form in the reaction mixture, and thermal decomposition of the first of these on distillation at atmospheric pressure (V).

We note also that under the conditions indicated above for the preparation of benzoyloxytrichlorosilane and after the termination of this reaction (as shown by cessation of evolution of hydrogen chloride) we determined the amount of distilled silicon tetrachloride and established that only such an amount of it enters the reaction with benzoic acid as is called for by the stoichiometric proportion in Equation (I).

In our previous studies carried out jointly with G. B. Eliakov it was shown that tetraacyloxysilanes are excellent reagents for acylation of the nuclei of benzene [5], thiophene [6-8] and selenophene [9, 10]. The very possibility of the utilization of tetraacyloxysilanes for acylation of benzene according to the Friedel-Crafts reaction was first shown by K. D. Petrov and co-workers [11, 12].

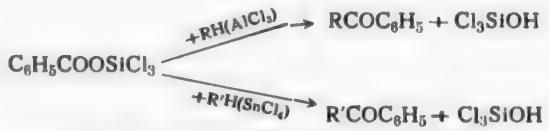
In connection with the above it appeared rather interesting, during the study of reactivity of benzoyloxytrichlorosilane, to study the possibility of acylation of compounds of aromatic nature by means of this substance. We ran an acylation of benzene with benzoyloxytrichlorosilane in the presence of anhydrous aluminum chloride and obtained benzophenone in yield of 73% (63.5% recalculated on the acid used to prepare benzoyloxytrichlorosilane). Since the distillation of benzoyloxytrichlorosilane, as indicated above, is accompanied by a slight decomposition, we ran the acylation of benzene with unpurified preparation, from which we only distilled the excess silicon tetrachloride under reduced pressure. In this case benzophenone was formed in a 70% yield, calculated on the acid used in the reaction with silicon tetrachloride. This fact indicates that benzoyloxytrichlorosilane proper is formed in nearly quantitative yield and that the yield of the pure substance amounts to only 88%, solely owing to the partial decomposition during distillation.

Thus, acylation of compounds of aromatic nature may be run also with undistilled benzoyloxytrichlorosilane, after the distillation from it of the excess silicon tetrachloride.

We obtained an 82% yield of a mixture of 2- and 4-methylbenzophenones by acylation of toluene with benzoyloxytrichlorosilane, from which mixture we isolated a 53% yield of 4-methylbenzophenone by repeated freezing-out, distillation and crystallization.

We obtained 2,4-dimethylbenzophenone (68%) by acylation of m-xylene.

Acylation of thiophene in the presence of anhydrous stannic chloride led to isolation of benzothienone in 70% yield.



$R = C_6H_5,\ CH_3C_6H_4,\ (CH_3)_2C_6H_3;\ R' = (C_4H_3S).$

It was interesting also to compare the reactivity of the benzoyloxy group and chlorine atoms in benzoyloxytrichlorosilane. It is known from the literature that during the action of alcohols on silicon tetrachloride, the chlorine atoms of the latter are readily replaced by the alkoxy groups with successive formation of alkoxytrichloro-, dialkoxydichloro-, trialkoxychloro- and tetraalkoxysilanes [13]. However the acyloxy group is also readily displaced by the alkoxy group, which was demonstrated by the reaction between butyl alcohol and methyltriacetoxysilane, which led to the formation of methylbutoxydiacetoxysilane and methyldibutoxyacetoxysilane [14].

We examined the action of ethyl alcohol on benzoyloxytrichlorosilane and established that the benzoyloxy group is replaced by the ethoxy group considerably more readily than are the chlorine atoms. To this fact we have the testimony of formation of benzoic acid in 69.5% yield, while molar amounts of the reactants were brought together at −25° to −30°. If the reactivities of the indicated groups were the same, the yield of the acid would have been but 25%.

At molar ratios of benzoyloxytrichlorosilane to ethyl alcohol of 1 : 3 and 1 : 4 the benzoic acid was obtained in yields of 80% and 88%, respectively, and along with it there was obtained tetraethoxysilane in yields of 38.5% and 45%, respectively.

$$C_6H_5COOSiCl_3 \begin{cases} \xrightarrow{+C_2H_5OH} C_6H_5COOH + C_2H_5OSiCl_3 + (C_2H_5O)_2SiCl_2 + HCl \\ \xrightarrow{+4C_2H_5OH} C_6H_5COOH + (C_2H_5O)_4Si + 3HCl \end{cases}$$

EXPERIMENTAL

Preparation of benzoyloxytrichlorosilane: a) Into a flask with a reflux condenser there was placed benzoic acid and silicon tetrachloride and the mixture was heated on a water bath until hydrogen chloride ceased to form. After distillation of the unreacted silicon tetrachloride the residue was distilled in vacuum. The results obtained in these experiments are shown in the table.

Expt. No.	Reaction components				Duration of heating the mixture (hours)	Amount of unreacted $SiCl_4$		$C_6H_5COOSiCl_3$ isolated		
	C_6H_5COOH		$SiCl_4$							
	in g	in moles	in g	in moles		in g	in moles	in g	in % of theory	b.p. (pressure in mm)
1	12.2	0.1	29.6	0.17	12	8.9	0.052	22.3	87.5	112—113° * (12)
2	12.2	0.1	34.0	0.20	12	17.0	0.10	22.5	88	116—117 (13)
3	12.2	0.1	34.0	0.20	5	22.1	0.13	9.2	36	107—108 (10)

*Found %: Si 10.76, 10.81; Cl 41.58, 41.57. $C_7H_5O_2Cl_3Si$. Calculated %: Si 10.98; Cl 41.65.

After five hours of heating the reaction mixture and allowing it to stand 12 hours at room temperature (table, expt. 3) there precipitated some crystals (0.7 g) which were tetrabenzoyloxysilane with m. p. 41-42°; mixed melting point with authentic tetrabenzoyloxysilane gave no depression. Literature data: m. p. 42° [15].

b) To dry tetrabenzoyloxysilane, prepared by the method of K. D. Petrov and E. S. Lagucheva [9] from 12.2 g (0.1 mole) of benzoic acid and 5 g (0.03 mole) of silicon tetrachloride in 100 ml of dry benzene, there was added (after removal of benzene in vacuum) 30 g (0.175 mole) of silicon tetrachloride and the reaction mixture was heated for 12 hours on a water bath. After distillation of the unreacted silicon tetrachloride, the residue was distilled in vacuum. There was obtained 13.7 g (53.5%) of benzoyloxytrichlorosilane, b. p. 112-113° (12 mm).

Preparation of benzoyl chloride. a) To dry tetrabenzoyloxysilane, prepared from 5.86 g (0.048 mole) of benzoic acid and 2.4 g (0.014 mole) of silicon tetrachloride in 20 ml of benzene, there was added (after distillation of benzene in vacuum) 6.1 g (0.024 mole) of benzoyloxytrichlorosilane and the mixture was subjected to

distillation at atmospheric pressure. There was obtained 6.6 g (64.5%) of benzoyl chloride, b. p. 194-195° (746 mm), $n^{20}D$ 1.5535, d^{20}_4 1.212.

b) Under analogous conditions from the reaction of tetrabenzoyloxysilane (from 5.86 g of benzoic acid and 2.4 g of silicon tetrachloride) and 12.2 g (0.048 mole) of benzoyloxytrichlorosilane there was obtained 3.25 g (0.02 mole) of silicon tetrachloride (b. p. 56-57°) and 8.5 g (63.5%) of benzoyl chloride (b. p. 194-195° at 747 mm, $n^{20}D$ 1.5533).

c) Distillation of 4.9 g (0.019 mole) of benzoyloxytrichlorosilane at atmospheric pressure gave 0.45 g (28%) of silicon tetrachloride (b. p. 56-57°) and 1.7 g (63%) of benzoyl chloride (b.p. 193.5-195° at 747 mm, $n^{20}D$ 1.5535).

Acylation of Aromatic Hydrocarbons and Thiophene by Benzoyloxytrichlorosilane

The reaction was run in a three neck flask (100 ml) with a stirrer and a reflux condenser with a calcium chloride tube (and a dropping funnel in case of acylation of thiophene).

Benzophenone. a) To the solution of 20 g (0.0785 mole) of benzoxyloxytrichlorosilane in 50 ml of dry benzene there was gradually addedin 3-4 g portions 18 g (0.13 mole) of dry aluminum chloride with the flask being cooled by ice water. Stirring was continued for 15 minutes at 20°, 5 hours at 30-40° and 15-20 minutes on a steam bath. The cooled mass was poured into ice and benzene was steam distilled. Benzophenone was distilled with superheated steam, the distillate was saturated with salt and extracted with ether. The ethereal extract was washed with alkali and water and was dried with anhydrous sodium sulfate. After distillation of the ether there was obtained 10.5 g (73% based on benzoyloxytrichlorosilane or 63.5% based on the benzoic acid taken for the synthesis of benzoyloxytrichlorosilane) of benzophenone with m. p. 45-47°. After distillation (b.p. 142° at 5 mm) benzophenone melted at 47.5-48°, and a sample mixed with an authentic specimen showed no depression.

b) A mixture of 12.2 g of benzoic acid and 29.6 g (0.17 mole) of silicon tetrachloride was heated for 12 hours on a water bath until cessation of evolution of hydrogen chloride. After the distillation of unreacted silicon tetrachloride (9.2 g, i.e., 0.054 mole) there was added to the liquid residue, which was benzoyloxytrichlorosilane, 50 ml of dry benzene followed by 18 g of dry aluminum chloride, as described above. There was obtained 13 g (70% of theoretical amount calculated on benzoic acid) of benzophenone, which after the above-described purification melted at 47.5-48°; a sample of it mixed with authentic benzophenone gave no depression.

4-Methylbenzophenone. To 25.5 g (0.1 mole) of benzoyloxytrichlorosilane there was added 50 ml of toluene; then 18 g of anhydrous aluminum chloride was added gradually as described above. After the appropriate treatment of the reaction mixture, the product was distilled in vacuum. There was obtained 16.05 g (82%) of a fraction with b.p. 140-150° (3 mm) consisting of a mixture of 2-methylbenzophenone with 4-methylbenzophenone. After repeated freezing-out, distillation and recrystallization, there was obtained 8.5 g (53%) of 4-methylbenzophenone with m.p. 57°. Literature data [11]: m.p. 57°.

Found %: C 85.83, 85.77; H 6.29, 6.27. $C_{14}H_{12}O$ Calculated %: C 85.69; H 6.17.

2,4-Dimethylbenzophenone. The synthesis of 2,4-dimethylbenzophenone was conducted as described above: from 25.5 g of benzyloxytrichlorosilane and 50 ml of m-xylene in the presence of 18 g of anhydrous aluminum chloride there was obtained 14.2 g (68%) of 2,4-dimethylbenzophenone:

B.p. 170° (11 mm), $n^{20}D$ 1.5918, d^{20}_4 1.1080. MR_D 64.21. $C_{15}H_{14}OF_6$. Calculated MR 64.58.
Found %: C 85.84, 85.68; H 6.79, 6.94. $C_{15}H_{14}O$. Calculated %: C 85.69; H 6.71.

Literature data [16]: b.p. 320°, d^{20}_4 1.0710.

Benzothienone. To 25.5 g of benzoyloxytrichlorosilane in 50 ml of dry benzene there was added 6.72 g (0.08 mole) of thiophene, after which 10.4 g (0.04 mole) of anhydrous stannic chloride in 20 ml of benzene was added dropwise with stirring. The mixture was heated for three hours on a water bath at 40-60° and for 15 minutes on a steam bath. There was obtained 10.5 g (70%) of benzothienone with m.p. 55-56°; m.p. 56-57° (from alcohol); mixed melting point with authentic benzothienone gave no depression. Literature data: m.p. 56.5-57° [17]; m.p. 55° [18], m.p. 56-57° [6].

Reaction of Benzoyloxytrichlorosilane With Ethyl Alcohol

a) To a solution of 17.1 g (0.067 mole) of benzoyloxytrichlorosilane in 30 ml of dry benzene cooled to −25° to −30° there was added dropwise 3.1 g (0.067 mole) of anhydrous ethyl alcohol, giving an immediate precipitate of benzoic acid. The mixture was stirred for five hours at 20° (evolution of hydrogen chloride) and the acid was filtered off. There was obtained 5.7 g (69.5%) of benzoic acid with m.p. 121-122°; a mixed specimen with authentic benzoic acid gave no depression.

After distillation of benzene from the filtrate there was obtained on the distillation of the residue a 4.7 g fraction with b.p. 101-120° and a 0.8 g fraction with b.p. 120-130°, in which according to the boiling points there was contained a mixture of ethoxytrichloro- and diethoxydichlorosilanes.

b) Under the same conditions there was obtained, from 25.5 g (0.1 mole) of benzoyloxytrichlorosilane in 30 ml of dry benzene and 13.8 g (0.3 mole) of anhydrous ethyl alcohol, 9.7 g (80%) of benzoic acid with m.p. 121-122°. After distillation of benzene from the filtrate and distillation of the residue there were obtained the following fractions: 1st b.p. 130-156° (740 mm), 2.4 g, and 2nd b.p. 89-90° (70 mm), 8 g.

The first fraction was a mixture of diethoxydichlorosilane and triethoxychlorosilane. The second fraction was tetraethoxysilane (yield 38.5%).

Found %: Si 13.23, 13.31. $C_8H_{20}O_4Si$. Calculated %: Si 13.47.

Literature data: b.p. 165-167° [19], b.p. 60-62° (12 mm) [20].

c) From 25.5 g (0.1 mole) of benzoyloxytrichlorosilane and 18.4 g (0.4 mole) of ethyl alcohol there was obtained 9.4 g of tetraethoxysilane (45%) with b.p. 89-90° (70 mm) and 10.8 g (88%) of benzoic acid with m.p. 121-122°.

SUMMARY

1. The reaction of benzoic acid with excess silicon tetrachloride yields benzoyloxytrichlorosilane.

2. The formation of benzoyl chloride from benzoic acid and silicon tetrachloride occurs as the result of the reaction of tetrabenzoyloxysilane and benzoyloxytrichlorisilane, the mixture of these being formed in the above reaction, and also as the result of the decomposition of the latter substance at elevated temperature.

3. Benzoyloxytrichlorosilane may be used as an acylating agent for acylation of the benzene nucleus (in the presence of anhydrous aluminum chloride) and for acylation of the thiophene nucleus (in the presence of anhydrous stannic chloride).

4. The benzoyloxy group in benzoyloxytrichlorosilane is more reactive than are the chlorine atoms and is more readily replaced by the ethoxy group during reaction with ethyl alcohol.

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SYNTHESIS OF UNDECYL AND DODECYLBENZENES AND THEIR PERHYDRIDES

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The first individual dodecylbenzene (3-methyl-1-phenylundecane) was synthesized for the purpose of studying the optical activity of its perhydrides [1]. Other isomers of it, as well as alkylbenzenes with lower molecular weights, were obtained in view of the interest they presented as hydrocarbon models of diesel fuels. In recent years the interest in dodecylbenzenes has increased considerably among investigators studying the effects of alkylbenzene structure on the wetting properties of sodium alkylbenzenesulfonates. Out of 3059 possible isomers of dodecylbenzene [2] only fourteen have been synthesized till now. Six of them (isomers with normal hydrocarbon chain and varying locations of the phenyl ring) were synthesized according to this scheme [3-5]:

$$C_6H_6 + RCOCl \xrightarrow{AlCl_3} C_6H_5COR \xrightarrow{R_1MgX} C_6H_5-\underset{\displaystyle R_1}{\overset{\displaystyle OH}{\overset{|}{\underset{|}{C}}}}-R \xrightarrow[+H_2]{-H_2O} C_6H_5-\underset{\displaystyle R_1}{\overset{|}{CH}}-R$$

We prepared 2-phenyldodecane through alkylation of benzene with dodecyl alcohol [6] or with dodecane-1 [7]; 1-phenyldodecane was obtained by Clemmensen [8] or Kishner [9] reduction of laurylphenone. The acylation step in the above described scheme can be replaced with oxidation of a corresponding alcohol to ketone [10]. Alkylbenzenes with quaternary carbon atoms next to the benzene were made by alkylating the latter with tertiary halides [11] or (as in the case of 2-methyl-2-phenylundecane, 4-methyl-4-phenylundecane, and 6-methyl-6-phenylundecane) with olefins possessing a double bond next to the tertiary carbon atom [12]. A series of isomers: previously mentioned 3-methyl-1-phenylundecane [1], 4-butyl-1-phenyloctane [13], 6-methyl-1-phenylundecane [14], and 2,8-dimethyl-5-benzylnonane [15] were synthesized in several steps using either Friedel-Crafts or Grignard reactions.

It is evident from this description that dodecylbenzenes with branched alkyl chains (i.e., hydrocarbon models of technical dodecylbenzene) have not yet been sufficiently studied. We synthesized hydrocarbons of composition C_{17} and C_{18} through the following reactions:

a) 1-Phenylalkane type

1. $C_6H_5CH_2CH_2COOC_2H_5 + 2C_4H_9MgBr \xrightarrow[+H_2]{-H_2O} C_6H_5CH_2CH_2CH(C_4H_9)_2$
2. $C_6H_5CH_2MgBr + (CH_3)_2CHCH_2CHBrC_6H_{13} \longrightarrow C_6H_5CH_2\underset{\displaystyle C_6H_{13}}{\overset{|}{C}}HCH_2CH(CH_3)_2$

b) 2-Phenylalkane type (two of them with quaternary carbon atoms next to the benzene ring)

3. $C_6H_5C(CH_3)_2CH_2MgCl + C_6H_{13}C\overset{O}{\underset{H}{<}} \xrightarrow[+H_2]{-H_2O} C_6H_5C(CH_3)_2CH_2C_7H_{15}$

4. $C_6H_5C(CH_3)_2CH_2MgCl + CH_3COC_6H_{13} \xrightarrow[+H_2]{-H_2O} C_6H_5C(CH_3)_2CH_2CHC_6H_{13}$ (CH$_3$ on the CHC$_6$H$_{13}$)

5. $C_6H_5COCH_3 + (CH_3)_2C{=}CHCH_2CH_2CH(CH_3)CH_2CH_2MgBr \xrightarrow[+H_2]{-H_2O}$
$\rightarrow C_6H_5CH(CH_3)CH_2CH_2CH(CH_3)CH_2CH_2CH_2CH(CH_3)_2$

And finally, we obtained a dodecylbenzene with maximum branching in the alkyl chain.

6. $C_6H_5Li + (CH_3)_3CCH_2C(CH_3)BrCH_2C(CH_3)_3 \rightarrow (CH_3)_3CCH_2C(C_6H_5)(CH_3)CH_2C(CH_3)_3$

The choice of these forms was dictated by the desire to find out whether highly or slightly branched homologs of technical dodecylbenzenes are preferable for the manufacture of wetting compounds. We determined solidification points and kinematic viscosities at 20 and 50° of all the hydrocarbons obtained by reactions 1-5. These data are listed in the Table, and n-dodecylbenzene (synthesized by Schmidt and co-workers [9]) is given for comparison. The solidification points of alkylbenzenes (in the 80-90° range) are on the average 5° lower than those of corresponding alkylcyclohexanes. One can see from the Table that the effect of hydrocarbon structure on the magnitude of kinematic viscosity at + 20°, and especially at + 50° is not very pronounced. At temperatures below zero the effect becomes much more apparent. Thus for hydrocarbon (VIII) ν_0 17.64, ν_{-20} 67.46, ν_{-40} 393.44; for (IX) ν_0 24.40, ν_{20} 105.70, ν_{40} 901.20.

EXPERIMENTAL

2,2,4,6,6-Pentamethyl-4-phenylheptane (II). a) Triisobutylene (made through polymerization of isobutylene in sulfuric acid) was treated over a long period of time with excess of hydrogen bromide at room temperature. Addition of hydrogen bromide was very slow. Vacuum distillation yielded a bromide, b.p. 99-101° (12 mm), $n^{20}D$ 1.4710, d^{20}_4 1.0572, which evidently had the 2,2,4,6,6-pentamethyl-4-bromopentane structure.

b) The whole dodecylbromide (30.5 g, 0.12 moles) was poured directly into an ether solution of phenyllithium; phenyllithium was made from 5.1 g (0.73 g-at.) of lithium and 57 g (0.36 moles) of bromobenzene, then separated from unreacted lithium. The reaction mixture was boiled for 3 hours, then part of the ether was distilled off, and heating was continued for 6 more hours at 70°. We isolated from the reaction mixture 10 g (30%) of dodecylbenzene in the normal way; its properties are listed in the Table. The structure ascribed to this hydrocarbon is based only on the fact that 90% of triisobutylene (prepared from isobutylene with sulfuric acid) is composed of two isomers: 1,1-dineopenthylethylene and 2,2,4,6,6-pentamethylheptene-3 [16].

2,4-Dimethyl-2-phenyldecane (III). a) An ether solution of a Grignard reagent was prepared from 337 g (2 moles) of 1-chloro-2-methyl-2-phenylpropane and 73 g (3 g-at.) of magnesium; to this solution we added 197 g (1.5 moles) of methylhexylketone. (We prepared 1-chloro-2-methyl-2-phenylpropane in a 78% yield through alkylation of benzene with methallyl chloride in sulfuric acid.) After boiling for 6 hours we decomposed the reaction mixture with water and 5% hydrochloric acid. We isolated 235 g (60%) of 2,4-dimethyl-2-phenyldecanol-4 from its ether solution.

B.p. 143-144° (2.5 mm), $n^{20}D$ 1.4918, d^{20}_4 0.9064, MR_D 83.87; calc. 83.75.
Found %: C 82.26; H 11.49. $C_{18}H_{30}O$. Calculated %: C 82.38; H 11.52.

b) A mixture containing 100 g (0.25 moles) of 2,4-dimethyl-2-phenyldecanol-4 and 178 g of 60% sulfuric acid was refluxed until the organic layer became transparent. Distillation over metallic sodium yielded 66 g (71%) of 2,4-dimethyl-2-phenyldecene.

B.p. 129-130° (2 mm), $n^{20}D$ 1.4950, d^{20}_4 0.8756, MR_D 81.38; calc. 81.85.

c) We hydrogenated 60 g of 2,4-dimethyl-2-phenyldecene at 120 atm in an autoclave over Raney nickel (10 g). The 2,4-dimethyl-2-phenyldecane (properties listed in the Table) obtained did not decolorize an alcoholic solution of bromine.

5,9-Dimethyl-2-phenyldecane (IV). a) We prepared 164.5 g (0.75 moles) of 3,7-dimethyl-1-bromooctene-6 from citronellol and phosphorus tribromide and added it slowly to 30.5 g (1.2 g-at.) of magnesium placed in ether. We added to the Grignard reagent 120 g (1 mole) of acetophenone over a period of 4 hours, then refluxed the reaction mixture for 10 hours. We decomposed the reaction mixture with water and vacuum distilled the ether solution; we isolated 120 g (66%) of 5,9-dimethyl-2-phenyldecadiene (dehydration product of a tertiary alcohol).

B.p. 162-164° (4 mm), $n^{20}D$ 1.5125, d^{20}_4 0.8843, MR_D 82.66; calc. 81.27.
Found %: C 88.43; H 10.97. $C_{18}H_{26}$. Calculated %: C 88.86; H 11.14.

b) We hydrogenated 76 g of 5,9-dimethyl-2-phenyldecadiene (mixed with 120 g of methyl alcohol) over Raney nickel (15 g) at 40° and 125 atm. The properties of 5,9-dimethyl-2-phenyldecane are listed in the Table.

2-Methyl-4-hexyl-5-phenylpentane (V). Benzene magnesium chloride was prepared from 185 g (1.4 moles) of chlorobenzene and 48 g (2 g-at.) of magnesium in ether. After removal of unreacted magnesium, 166 g (0.7 moles) of 2-methyl-4-bromodecane was added all at once to the organomagnesium compound at room temperature. No visible signs of reaction were observed. Most of the ether was distilled off, and the contents of the flask heated for 6 hours at 90-100°; after this, the ether which was previously distilled off was poured back into the flask and the reaction mixture decomposed with water. We isolated 116 g (67%) of 2-methyl-4-hexyl-5-phenylpentane from the ether solutions.

2-Methyl-4-phenyldecane (VI). a) We added 167 g (1.5 moles) of heptanol to an organomagnesium compound prepared from 200 g (1.2 moles) of 1-chloro-2-methyl-2-phenylpropane and 48.6 g (2 g-at.) of magnesium. We isolated 180 g (60%) of 2-methyl-2-phenyldecanol-4 from the reaction mixture in the usual way.

B.p. 149-150° (2 mm), $n^{20}D$ 1.5003, d^{20}_4 0.9281, MR_D 78.65, calc. 79.10.
Found %: C 82.90; H 11.30. $C_{17}H_{28}O$. Calculated %: C 82.19; H 11.36.

b) We boiled 145 g of 2-methyl-2-phenyldecanol-4 for 15 hours in 217 g of 60% H_2SO_4. We obtained 109 g (81%) of 2-methyl-2-phenyldecene.

B. p. 136-137° (5.5 mm), $n^{20}D$ 1.4982, d^{20}_4 0.8740, MR_D 77.20; calc. 77.10.
Found %: C 88.70; H 11.30. $C_{17}H_{26}$. Calculated %: C 88.63; H 11.37.

c) We mixed 105 g of 2-methyl-2-phenyldecene with 140 g of methyl alcohol and hydrogenated over 20 g of Raney nickel in a liter autoclave. The initial pressure was 132 atm, temperature 20°. The 2-methyl-2-phenyldecane previously obtained [17] from bromooctane and phenylisopropyl potassium had the following properties: $n^{20}D$ 1.4859, d^{20}_4 0.8676, b.p. 160° (20 mm).

3-Butyl-1-phenylheptane (VII). To an ether solution of butylmagnesium bromide (made from 274 g (2 moles) of butyl bromide and 62 g (2.5 g-at.) of magnesium) slowly we added 134 g (0.75 moles) of ethyl hydrocinnamate. The reaction mixture was boiled for 6 hours and decomposed with water. We isolated 146 g (78.5%) of 3-butyl-1-phenylpentanol-3 from its ether solution.

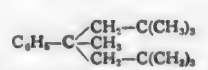
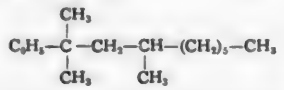
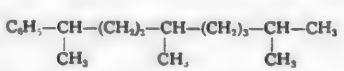
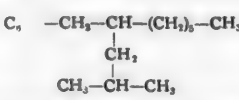
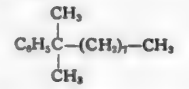
B.p. 140-142° (3 mm), $n^{20}D$ 1.5000, d^{20}_4 0.9261, MR_D 78.89; calc. 79.10.
Found %: C 82.20; H 11.40. $C_7H_{28}O$. Calculated %: C 82.19; H 11.36.

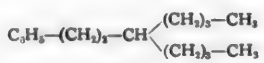
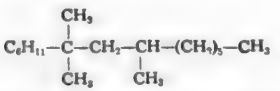
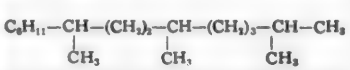
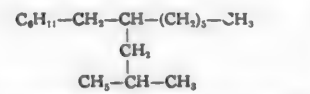
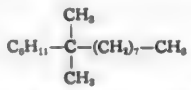
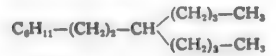
b) We boiled 126 g of 3-butyl-1-phenylheptanol-3 for 3 hours with 200 g of 60% sulfuric acid. As a result we obtained 108 g (92.5%) of 3-butyl-1-phenylheptene.

B.p. 116-118° (2 mm), $n^{20}D$ 1.4980, d^{20}_4 0.8793, MR_D 76.77; calc. 77.10.
Found %: C 87.98; H 11.26. $C_{17}H_{26}$. Calculated %: C 88.63; H 11.37.

c) We hydrogenated 98 g of 3-butyl-1-phenylheptene in a liter autoclave over 15 g of Raney nickel; the initial pressure was 120 atm, temperature 50°. The properties of the alkylbenzene obtained are listed in the Table.

Hydrogenation of dodecyl and undecylbenzenes (II-V). Hydrogenation was carried over Raney nickel at 180-200° under a 200-220 atm pressure. To ascertain the purity of dodecyl and undecylcyclohexanes obtained, we took ultraviolet spectrum of hydrogenated 2-methyl-2-phenyldecane and were unable to detect the characteristic benzene lines.

Substances	Compound	Boiling point (pressure in mm)	Solidification point	n_D^{20}	d_4^{20}	MR_D calc. from atoms	MR_D calc. from comp.	MR_D found	Viscosity (in centistokes) 20°	Viscosity (in centistokes) 50°	Found* % C	Found* % H
(I)	$C_6H_5-CH_2-(CH_2)_{10}-CH_3$[9] Dodecylbenzene	183—185° (12)	—	1.4822	0.8364	81.72	82.23	82.06	6.294	3.191	—	—
(II)	 2,2,3,6,6-Pentamethyl-4-phenylheptane	133—135 (14)	—	1.4930	0.8811	81.72	82.23	81.28	—	—	88.10, 88.00	12.10, 12.10
(III)	 2,4-Dimethyl-2-phenyldecane	136—136.5 (5)	—89 ст	1.4850	0.8637	81.72	82.23	81.74	6.896	3.288	87.52, 87.74	12.40, 12.41
(IV)	 5,9-Dimethyl-2-phenyldecane	134—135 (2)	—82 ст	1.4815	0.8553	81.72	82.23	82.05	8.012	3.533	87.64, 87.60	12.38, 12.29
(V)	 2-Methyl-4-hexyl-5-phenylpentane	130.5 (3)	—81 ст	1.4889	0.8657	81.72	82.23	82.14	6.794	3.007	88.07, 87.92	11.80, 11.80
(VI)	 2-Methyl-2-phenyldecane	146.5 (2)	—93 ст	1.4881	0.8665	77.11	77.58	77.28	6.528	3.015	87.96, 87.75	12.06, 11.98

(VII)	 3-Butyl-1-phenylheptane	134 (3)	—97 ст	1.4839	0.8569	77.11	77.58	77.58	5.160	2.450	87.62, 87.75	12.23, 12.12
(VIII)	 2,4-Dimethyl-2-cyclohexyldecane	134—135 (2)	—83 ст	1.4778	0.8546	83.12	83.51	83.60	7.551	3.627	—	—
(IX)	 5,9-Dimethyl-2-cyclohexyldecane	140—141 (3)	—79 ст	1.4698	0.8442	83.12	83.51	83.41	8.776	3.701	—	—
(X)	 2-Methyl-4-hexyl-5-cyclohexyl-pentane	138—139 (5)	—75 ст	1.4659	0.8375	83.12	83.51	83.47	9.126	3.779	—	—
(XI)	 2-Methyl-2-cyclohexyldecane	124—125 (2)	—86 ст	1.4764	0.8540	78.50	78.86	78.81	7.493	3.297	—	—
(XII)	 3-Butyl-1-cyclohexylheptane	134—135 (4)	—92 ст	1.4570	0.8252	78.50	78.86	78.67	9.360	3.870	—	—

*Substances (II-V) $C_{19}H_{30}$. Calculated %: C 87.72; H 12.28. Substances (VI-VII) $C_{17}H_{28}$. Calculated %: C 87.87; H 12.13.

SUMMARY

A series of undecyl, dodecylbenzenes and their perhydrides was synthesized. Kinematic viscosities and solidification points were determined for the synthesized hydrocarbons.

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RESEARCH IN THE FIELD OF SYNTHESIS AND CONDENSATION OF N-ALKYL DERIVATIVES OF HEXAMETHYLENEDIAMINE

V. REACTION MECHANISM OF REDUCTIVE ALKYLATION OF HEXAMETHYLENEDIAMINE

A. L. Klebanskii and M. S. Vilesova

In order to clarify the reaction mechanism of reductive alkylation of hexamethylenediamine, it was necessary to consider the problem of possible intermediate products and the role of catalyst.

It is generally accepted that an azomethine base (Schiff's base) is formed as an intermediate in the reductive alkylation [1]. In order to find out if a Schiff's base was present as an intermediate product, we compared the reduction rate of a hexamethylenediamine–butyraldehyde mixture with that of a corresponding azomethine base:

$$CH_3CH_2CH_2CH=N(CH_2)_6N=CHCH_2CH_2CH_3$$

both rates were measured in an alcoholic solution. In Fig. 1 we showed that the reduction of the above mentioned mixture proceeds much faster than that of pure Schiff's base. Since the slowest stage determines the over-all reaction rate, it is obvious that an azomethine base could not be an intermediate product in the reductive alkylation.

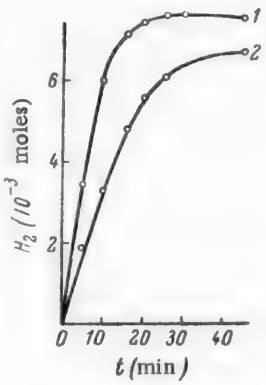
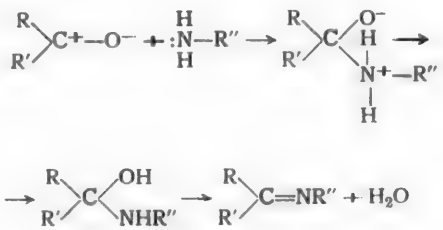


Fig. 1. Reduction of hexamethylenediamine–butyraldehyde mixture (Curve 1), and of a corresponding Schiff's base (Curve 2) under atmospheric pressure.

In connection with the question brought up above another one arose: what adducts could be present in a hexamethylenediamine–carbonyl compound mixture before reduction takes place? In accordance with the usual electronic representation [2], the interaction of an aldehyde or ketone with an amine can be illustrated by the following scheme:



According to this scheme we would expect that besides starting materials, hydroxyl containing products and Schiff's bases would be present in the reaction mixture. Since, as the kinetic data would indicate, Schiff's base could not be an intermediate (but if it was, it would not be the only intermediate to determine the whole reaction rate), a doubt arose if it was formed at all under mild conditions; maybe the hydroxyl compound is an intermediate and is catalytically reduced.

To answer this question, we obtained some infrared spectra of starting materials, of their mixture, and of a corresponding Schiff's base (Fig. 2) in the 1400-1800 cm^{-1} regions (an IKS-11 spectrometer with a rock salt

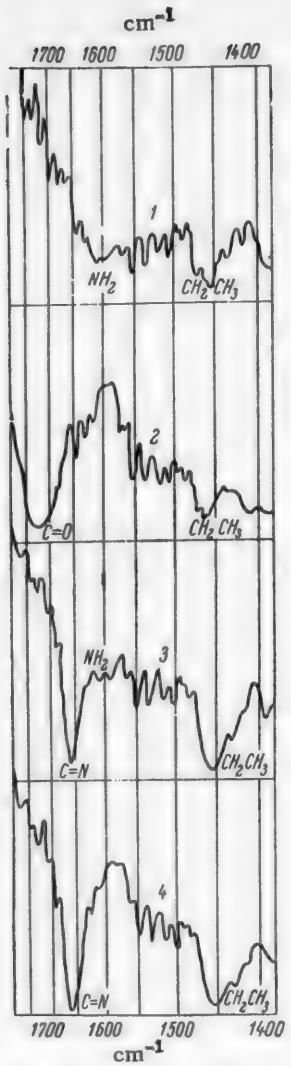


Fig. 2. Infrared spectra. 1) Hexamethylenediamine; 2) butyraldehyde; 3) hexamethylenediamine–butyraldehyde mixture; 4) Schiff's base.

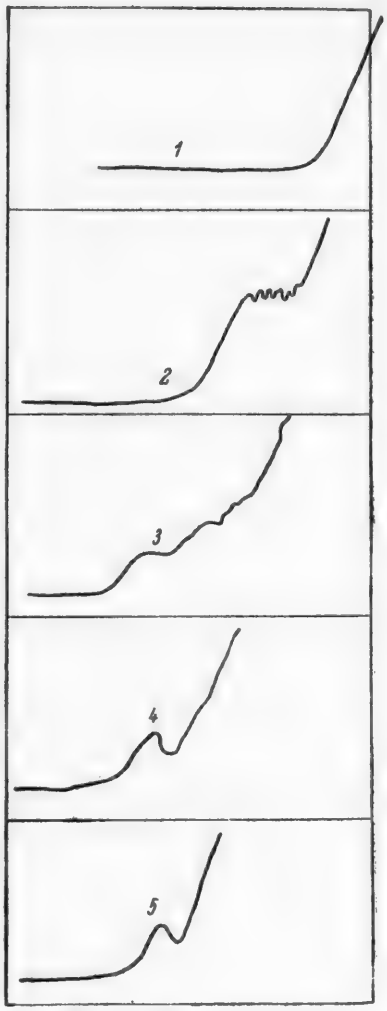


Fig. 3. Polarograms. 1) Hexamethylenediamine (in 0.1 N LiOH); 2) butyraldehyde (in 0.1 N LiOH); 3) hexamethylenediamine–butyraldehyde mixture (in 0.1 N LiOH); 4) same mixture (in absolute alcohol); 5) Schiff's base (in absolute alcohol).

prism was used). The spectra of initial diamine and butyraldehyde show vibrational absorption bands corresponding to the NH_2 and C=O bonds respectively. A very intense band was observed at a frequency of 1668 cm^{-1}; this band corresponds to the C=N bond vibration and was absent in the starting material. The same frequency was observed in the spectrum of Schiff's base. The mixtures also showed a very intense absorption in the region corresponding to a OH bond vibration (3500-3700 cm^{-1}). However, it was hard to decide whether it was due to the presence of H_2O (water is split out when Schiff's base is formed), or the presence of hydroxyl-containing compounds formed as a result of diamine addition to the aldehyde. Spectra of acetone and its mixture with hexamethylenediamine were also obtained; these fully matched the spectra obtained for butyraldehyde and its mixture with the same amine.

The above mentioned spectroscopic data* would indicate that in a diamine–carbonyl compound mixture a Schiff's base is rapidly formed. We were not able to detect any hydroxyl-containing intermediates by comparing the spectrum with that of a compound approximately resembling it structurally: $R-CHOH-CH_2-NHCH_3$.

A hydroxyl intermediate ($R'R''COH-NH-(CH_2)_6-NH-COHR'R''$) must exist in the formation of an azomethine base; however, it evidently is unstable (because of two functional groups on one carbon) and is immediately converted into a Schiff's base as soon as it is formed. Hence, for the reason just stated, there is no ground to consider it an intermediate in solution.

A supplementary polarographic study of individual compounds and their mixtures carried in solution** confirmed the spectroscopic data qualitatively (spectra were made without solvents). One can see on the polarograms (Fig. 3, Curve 1), that hexamethylenediamine is not reduced on a mercury-drop electrode and its polarogram looks straight. Butyraldehyde gives a strong reduction wave (Fig. 3, Curve 2). The diamine–aldehyde mixture gives two waves; the first one corresponds to the newly formed compound, the second one to the remaining unreacted butyraldehyde (Curve 3). The polarogram of Schiff's base has a reduction wave which is identical with the one found in the mixture, and which is due to the C=N linkage (Curve 4). The data obtained showed that besides remaining free starting materials, a Schiff's base is also formed when a diamine–carbonyl compound mixture is dissolved in alcohol. The formation of a Schiff's base in a solution containing a mixture of diamine and carbonyl compound is not a sufficient basis for considering it the primary intermediate product in the reductive alkylation, for this idea would be inconsistent with the kinetic data on the reduction rate of the mixture and of a corresponding Schiff's base.

One could assume that if starting materials are chemisorbed much faster on the catalyst then are Schiff's bases, then this would constitute a decisive factor in making the catalytic reduction rate of the mixture greater than that of the corresponding azomethine base.

We set up experiments whereby azomethine bases and corresponding diamine–aldehyde mixtures could be reduced with atomic hydrogen (nascent) without utilizing a catalyst; this would exclude any effects which a catalytic absorption of reaction constituents might have on the course of reductive alkylation. Two variations of the experiment were used: with Na in ethanol, or with Zn in dilute HCl; the data on the reduction rates (based on the determination of the number of unsubstituted amino groups) are listed in the Table, and it is evident that in this case the Schiff's base was hydrogenated much faster than the mixture (in contrast to the catalyzed process). The reaction rate depends on the concentration of Schiff's base, and in the case of the mixture it should be determined by the rate at which C=N bonds are formed. The experiments in which reduction was done by nascent hydrogen indicate also, that the concentration of Schiff's base as a diamine–aldehyde mixture is not large under these conditions (dilute solutions, acidic or alkaline medium).

Reduction of Hexamethylenediamine–Butyraldehyde Mixture and a Corresponding Schiff's Base With Nascent Hydrogen

The substance reduced	Conditions of reduction	The amount of product that reacted after 3 hrs. (in %)
Schiff's base	Zn + HCl	87
Mixture	Zn + HCl	9
Schiff's base	Na + C_2H_5OH	91
Mixture	Na + C_2H_5OH	10

Thus, on the basis of the cited experimental material one can assume that a diamine–carbonyl compound mixture contains not only the starting materials but also a small concentration of nascent Schiff's base (under catalytic reduction conditions). Kinetic experiments give no grounds for the assumption that the reaction

*Spectra were determined by L. D. Shcherba.

**Polarograms were determined by L. P. Seliutina.

proceeds through a stage at which Schiff's base is adsorbed from solution. The rate determining step in the reductive alkylation is the chemisorption of individual starting components (diamine and aldehyde or ketone) and subsequent interaction on closer approach on the active surface. In such a case the faster adsorption of the components will make the reduction rate of the mixture greater; the adsorption rate depends on polarizability, and Schiff's bases (which may be formed on the active surface) are much less polarizable than compounds with NH_2 and CO groups.

EXPERIMENTAL

1. Synthesis of an azomethine base. The reaction was conducted in a round-bottomed three-necked flask which was supplied with a mechanical stirrer, a thermometer, and a dropping funnel. We placed 58 g of hexamethylenediamine and added 76 g of butyraldehyde dropwise (flask was cooled with ice). We added 20 g of fused KOH to the reaction mixture. The reaction lasted 2 hours. At first the reaction warmed up to 75°, then it continued at room temperature. When it was terminated, we distilled off unreacted aldehyde, dissolved the mixture in 400 ml of ether, washed away unreacted diamine with water, and dried over K_2CO_3. After removal of ether, the residue was fractionally distilled under reduced nitrogen pressure. A constant boiling fraction, b.p. 119-121° (3 mm), was collected; it was a Schiff's base made of hexamethylenediamine and butyraldehyde.* We obtained 28 g (25%) of azomethine.

B.p. 119-121° at 3 mm, d^{25}_4 0.836, $n^{25}D$ 1.4539, MR_D 72.4; calc. 72.2.

Found %: N 12.5 (by Kjeldahl method); C=N 22.27 (by hydrogenation according to Willstätter). M 240 (method of Rast). $C_{14}H_{30}N_2F_2$. Calculated %: N 12.37; C=N 22.96. M 226.4.

Under the conditions of the Van Slyke determination of NH_2 content, Schiff's base is unstable and decomposes into a diamine and aldehyde.

2. Catalytic reduction of a hexamethylenediamine–butyraldehyde mixture, and of a corresponding Schiff's base. Experiments were conducted in a Willstätter duck-shaped apparatus under atmospheric pressure (method described in [3]). We used in this reduction 0.460 g of hexamethylenediamine in 23.8 ml of alcohol and 0.571 g of n-butyraldehyde (a 1:2 molar ratio). For the hydrogenation of Schiff's base we took 0.896 g of it in 23.9 ml of alcohol. The volume of mixture was 25 ml, the quantity of platinum oxide 0.1000 g, and the concentration of diamine or Schiff's base 0.160 moles/liter; these amounts were kept constant in both cases. The data on the absorption rate of hydrogen are shown in Fig. 1. Results were the same when experiments were carried out with double the concentration of diamine and Schiff's base.

3. Reduction of a hexamethylenediamine–butyraldehyde mixture, and of a corresponding Schiff's base using atomic hydrogen. The reaction was carried out in a two-necked flask supplied with a reflux condenser, a dropping funnel, and a stirrer; the temperature was kept 20 ± 0.1° in a thermostat. We placed an alcoholic or aqueous solution of hexamethylenediamine together with pieces of sodium or zinc powder in the flask; to this we added alcohol or hydrochloric acid (1:1), and as soon as hydrogen evolution began we turned the stirrer on and added (through a dropping funnel) a weighed portion of butyraldehyde or Schiff's base. The funnel was then rinsed out with whatever solvent was used in reaction. After 3 hours we stopped the reaction, separated the reaction mixture from residues, measured its volume, and analyzed for NH_2 groups. The number of substituted NH_2 groups was used as a control for this analysis.

We used 0.891 g of hexamethylenediamine and 1.108 g of butyraldehyde or 1.719 g of Schiff's base respectively. The quantity of solvent was 97 ml of ethyl alcohol or hydrochloric acid (1:1) for the mixture, and 98 ml of the same ones for hydrogenation of Schiff's base. In all the cases the volume of the reaction mixture was 100 ml. We used 10.0 g of sodium and 15.0 g of zinc powder. The concentration of diamine or Schiff's base was kept at 77×10^{-3} moles/liter in all the experiments. The experimental results are shown in the Table.

SUMMARY

1. The presence of Schiff's base in a hexamethylenediamine–butyraldehyde mixture was established with the help of infrared spectra and polarography.

*This compound has been obtained and characterized for the first time.

2. We established that the catalytic hydrogenation rate is greater for the diamine–aldehyde mixture than for a corresponding Schiff's base.

3. We showed that if hydrogenation is done with nascent hydrogen, then the reduction rate of Schiff's base is much greater than that of a hexamethylenediamine–carbonyl compound mixture.

4. A mechanism is offered for the reductive alkylation; according to it, the diamine and the carbonyl compound are chemisorbed individually on the catalyst, interact, and are reduced in the adsorbed state. The chemisorption rate of individual constituents will determine the rate of reductive alkylation. The reduction of the Schiff's base present in solution does not completely determine the course of reaction.

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RESEARCH IN THE FIELD OF SYNTHESIS AND CONDENSATION OF N-ALKYL DERIVATIVES OF HEXAMETHYLENEDIAMINE

VI. SYNTHESIS OF POLYAMINES STARTING WITH N-ALKYLATED HEXAMETHYLENEDIAMINE. PRODUCTION OF PARTLY N-ALKYLATED POLYAMIDES

A. L. Klebanskii and M. S. Vilesova

Fundamental properties of polyamides (crystallinity, tensile strength, stability in organic solvents et al.) indicate characteristically strong intermolecular interactions which are due to van der Waals forces and hydrogen bonding [1]. Due to the strong additive character of these linkages (whose total energy may exceed that of C—C bonds [2]) the intermolecular interaction among polyamides is consequently much greater than among a series of other synthetic polymers [3].

Briggs, Frosch, and Erickson [4] investigated the effect of the degree and regularity of N-methylation on the melting points of substituted polyamides; they connected their data with the degree of crystallinity in the polymer. Wittbecker et al. [5] have investigated a series of substituent radicals, and showed that an isobutyl-substituted polyamide of definite composition and with dispersed substituents constituted a substance with increased elasticity; some properties (determined in experiments conducted on threads) are close to those of synthetic rubber.

In order to disrupt the crystalline structure of polyamides and give them elastic properties, we obtained in this work a series of products, by starting with variously substituted (with respect to N or N') diamines and mixing them with unsubstituted diamines. When N,N'-disubstituted diamines are used in polycondensation, they form polyamides without intermolecular hydrogen bonds and with substantially weakened van der Waals interactions (which stipulates an balsam-like consistency in polycondensates); to these diamines we applied a special after-treatment with diisocyanates which leads to the formation of comparatively sparsely distributed bridged valence bonds. In this manner, two principally different types of polyamides were obtained. In the first one of these, polycondensation results in relatively short polymeric molecules, which are linked to each other through hydrogen bonds. The polymers of the second type are characterized by a complete absence of hydrogen bonding and by a lengthening of main polyamide chains; the lengthening is due to the reaction of end groups with diisocyanate and the presence of bridged valence bonds between chains (these are formed when diisocyanate reacts with carbamide groups formed on chain lengthening). These polymers are characterized by a straight chain structure; the properties can vary depending on the structure of substituents (size, branching), length of initial chain section, and finally, on the structure of the diisocyanate molecules themselves. Thus, the polymers of the second type present more possibilities for a guided modification of their chemical and physicomechanical properties (for the synthesis of this type of polymers see communication VII).

The synthesis of partially N-alkylated polyamides was accomplished through copolymerization of N,N'-di, N-monosubstituted, and unsubstituted adipamides in different proportions.

For the polycondensation with adipic acid (to obtain a partially N-substituted polyamide) we used N,N'-diisoprophylhexamethylenediamine and N-monoisopropylhexamethylenediamine out of a whole series of N-substituted diamines synthesized in this work. The choice of just these was determined for the following considerations: in the first place, the isopropyl group, having destroyed the hydrogen bond by replacing a hydrogen on the nitrogen, decreases the possibility of secondary phenomena (due to high branching and relatively short chain length) connected

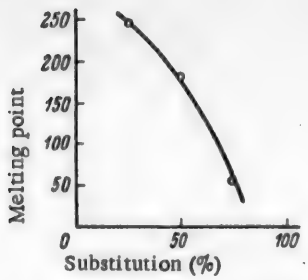

Fig. 1. Melting points of polyamides as a function of the degree of N-alkylation (as an example N-isopropyl substituted).

with orientation of a long substituent chain alongside the polymer chain [5], and with interaction of substituents themselves; in the second place, the synthesis of initial monomeric N-isopropylhexamethylenediamine derivatives proceeds smoothly with optimum yields and reaction rates, and also requires such a readily available product as acetone for alkylation.

Adipamides of the specific substituted diamines and of hexamethylenediamine were used as initial compounds in the polycondensation. These amides contained equimolecular quantities of diamine and dibasic acid; all crystallized nicely except the amide of N-monoisopropylhexamethylenediamine which separated out of solution as an oil. The polycondensation was conducted under the conditions usually used to obtain polyamides in the absence of a solvent [6].

In order to investigate the effect of degree of substitution on the properties of a polyamide, we polycondensed the following mixture: 1) 75% of hexamethylenediamine adipamide + 25% N,N'-diisopropylhexamethylenediamine adipamide. As compared to pure AH* polycondensation product, this polymer should theoretically contain 25% N-substituted groups. 2) We used 50 mole % hexamethylenediamine adipamide + 50 mole % N,N'-diisopropylhexamethylenediamine adipamide. 3) We used 25 mole % hexamethylenediamine adipamide + 75 mole % N,N'-diisopropylhexamethylenediamine adipamide. Depending on the degree of substitution, the polyamides are conventionally designated as: "N-isopropyl-substituted 75 : 25, 50 : 50, 25 : 75" respectively.

A polyamide was prepared through polycondensation of N-monoisopropylhexamethylenediamine with adipic acid (in equimolar ratio) so as to compare the effectiveness of substitution with respect to the relative amounts of N,N'-di- or N-monoalkylated diamines in the polymer structure (at an equal over-all degree of N-substitution, 50%); its properties are compared with those of a "N-isopropyl-substituted 50 : 50" polyamide obtained through polycondensation of a N,N'-disubstituted and unsubstituted diamine mixture with adipic acid.

We have established that as the number of N-substituted groups increases, a greater solubility in a series of organic solvents becomes apparent. The melting point of polymers is lowered too (Fig. 1). A comparison of properties among polyamides obtained by using N,N'-di- and N-monosubstituted diamines at an equal over-all degree of substitution shows that the use of N-monosubstituted diamine results in the formation of a product which is characterized by a lowered melting point, an increased solubility in organic solvents (in comparison to a product based on N,N'-disubstituted diamine), and a lack of brittleness at ordinary temperatures (Table 1).

TABLE 1

The Effect of Substitution Sequence on the Properties of Polyamides

N-isopropyl substituted polyamide (50% substitution)	Melting point	Solubility	
		ethyl alcohol	acetone
Based on N,N'-disubstituted diamine	185°	–	–
Based on N-monosubstituted diamine	74	+	+

The differences shown in the properties of polyamides could be explained by variations in the degree of regularity in the chain structure, depending on whether N-mono- or N,N'-dialkylated diamines were used.

EXPERIMENTAL

The polycondensation process was carried out in an apparatus shown in Fig. 2. The pyrex apparatus was assembled from sections and consisted of: a reaction flask, an adapter supplied with an electric heater, and a

*AH is an accepted abbreviation for hexamethylenediamine adipamide.

thermally insulated column packed with glass coils. An extension tap to connect the apparatus to a vacuum system through an outlet could replace the column. A capillary was lowered into the reaction flask for the purpose of bubbling nitrogen, since the polycondensation was conducted under a nitrogen atmosphere. Such an apparatus had been used [7] for the synthesis of polyesters. The nitrogen was carefully purified from hydrogen and dried with concentrated sulfuric acid and phosphorus pentoxide. The apparatus was heated in a ditolylmethane bath. Hexamethylenediamine, N,N'-diisopropylhexamethylenediamine, and N-monosiopropylhexamethylenediamine adipamides were the starting materials in the polycondensation. The preparation of amides was reduced to the following operations. Adipic acid was dissolved in ethyl alcohol with heating. Next, a 5% excess of diamine (over 1 : 1 acid-diamine ratio) was added to the solution, the mixture was heated to the boiling point of water bath, and after completion cooled in ice. At this stage crystalline amide precipitated. This amide was washed with ethyl alcohol on a suction funnel and dried at 100°. The amide of N-mono-substituted diamine did not crystallize, but settled out as an oil.

To 58.4 g of adipic acid in 100 ml of ethyl alcohol we added 48.7 g of hexamethylenediamine. We obtained 96.2 g of amide (92% yield from the acid used in reaction). M.p. 190°.

To 58.4 g of adipic acid in 135 ml of ethyl alcohol we added 84.0 g of N,N'-diisopropylhexamethylenediamine. We obtained 131.4 g (95%) of amide. M.p. 168°.

To 58.4 g of adipic acid in 120 ml of ethyl alcohol we added 66.3 g of N-monoisopropylhexamethylenediamine. We obtained 105.8 g of amide (in the form of an oil), yield 87%.

In all the cases (computed from molecular weights) the molar diamine–acid ratio was 1 : 1 in the salts prepared.

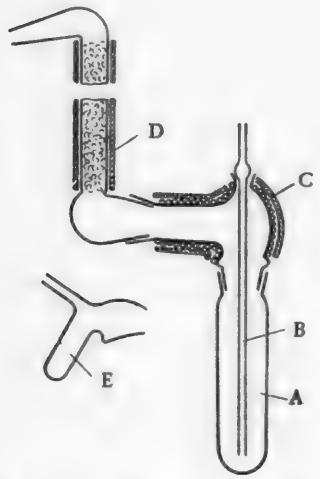

Fig. 2. Apparatus for conducting polycondensation reactions.
A) Reaction vessel; B) capillary; C) adapter; D) column; E) an extension tap for connecting to a vacuum system.

The polycondensation experiments were conducted in the following manner. A mixture of amides was placed in the reaction flask. The apparatus was lowered into a bath, the heat was turned on, and nitrogen was bubbled through. Since the amides were nonvolatile we had no use for the packed column and right away hooked to the apparatus the extension tap into which went the water formed in the reaction. The bath temperature was raised to 220° and the mixture kept at this temperature until no more water was being driven off. The adapter was heated with a coil to prevent water from condensing and returning into the reaction flask. The apparatus was then connected to a vacuum system, suction was applied, and gradually the residual pressure was reduced to 0.8-0.4 mm. The bath temperature was gradually increased so as to keep all the polymers liquid and allow nitrogen bubbles to pass through the reaction mixture. The reaction was judged to be complete when the weight of reaction mixture ceased diminishing (the apparatus with capillary and adapter was weighed under nitrogen) after cooling. After completion of reaction, the polymers were poured out into porcelain evaporating dishes and cooled in a desiccator. Table 2 lists the ratios of components used in the polycondensation for the purpose of getting polyamides possessing various degrees of alkylation. The reaction was conducted for 20 hours at atmospheric pressure and 220°, and for 10 hours at the final 0.4 mm pressure and 250°. Table 3 shows other characteristic properties of polyamides obtained by us.

All the investigated N-alkylated polyamides are soluble in formic acid, insoluble in water, ether, petroleum ether, and benzene. Only N-isopropyl-substituted 25 : 75 and N-isopropyl-substituted 50 : 50 (with regular structure) are soluble in ethyl alcohol.

TABLE 2

Experimental Data From the Preparation of N-Alkylated Polyamides

Amide AH (g)	Adipamide of N-substituted hexamethylenediamine	Weight (in g)	Ratio AH : amide of substituted diamine	Designation of polyamide
21.00	N,N'-Diisopropylhexamethylenediamine	9.25	75 : 25	N-Isopropyl-substituted 75 : 25
12.00	The same	15.90	50 : 50	The same 50 : 50
6.00	The same	23.68	25 : 75	The same 25 : 75
–	N-Monoisopropylhexamethylenediamine	28.00	0 : 100	The same 50 : 50 with regular structure

TABLE 3

Some Properties of N-Alkylated Polyamides

Polyamides	Melting point (following Kramer-Sarnov)	Viscosity (η)		Remarks
		specific of 3.0% alcoholic solution	absolute	
N-Isopropyl-substituted 75 : 25	248°	–	–	Hard, brittle
N-Isopropyl-substituted 50 : 50	185	–	–	Same
N-Isopropyl-substituted 25 : 75	54	0.561	0.170	Soft, possesses some elasticity
N-Isopropyl-substituted 50 : 50 with regular structure	74	0.682	0.166	Same

SUMMARY

1) By starting with N,N'-di- and N-monoisopropylhexamethylenediamine and adipic acid we obtained and characterized polyamides with a varying degree and sequence of N-substitution.

2) We have established that an increase in degree of substitution improves the solubility of polyamides, gradually lowers the melting point, and decreases the brittleness of polymers. Regular substitution is more effective as compared to irregular of the same degree.

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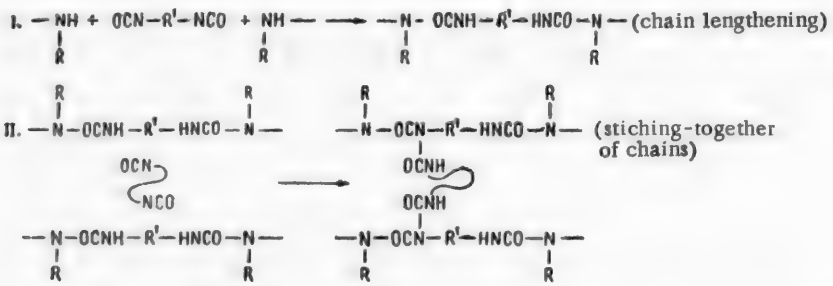
A STUDY IN THE FIELD OF SYNTHESIS OF N-ALKYL DERIVATIVES OF HEXAMETHYLENEDIAMINE AND THEIR POLYCONDENSATION

VII. PREPARATION OF COMPLETELY N-ALKYLATED POLYAMIDES AND COUPLING OF THEIR CHAINS WITH A DIISOCYANATE

A. L. Klebanskii and M. S. Vilesova

The use of diisocyanates for lengthening or "stitching-together" of chains of polyesters has been described extensively [1]. This method is used here for the first application to N-substituted polyamides and is used in two stages: 1) the preparation of completely N-substituted polyamides from adipic acid and N,N'-dialkylhexamethylenediamine with various substituents as the radicals, and 2) the lengthening of the chains of the resulting polyamide and the transformation of the linear polymer into a tridimensional polymer by the reaction with a diisocyanate according to the reaction scheme:



Thus, the first stage consists of the preparation of a polyamide based on a N,N'-dialkylated diamine which leads to the formation of a completely N-substituted polymer which is characterized by the lowered intermolecular interaction as a result of the introduction of the substituents at the nitrogen, which totally destroy the hydrogen bonds and reduce the van der Waals forces.

In order to insure the formation of the link of the polyamide chains (during their lengthening) by the diisocyanate predominantly with the typical carbamido links, it was necessary to prepare a polymer with secondary amino groups at the chain ends. In a case in which the ends of the polyamide chains are terminated by carboxyl groups the link with the diisocyanate would be formed in the shape of an amide linkage and would be accompanied by evolution of carbon dioxide which is naturally undesirable owing to the formation of pores in the polymer mass. For preparation of a polyamide with terminal secondary amine groups there was taken an excess of the diamine for the polycondensation reaction. In connection with this, the starting reaction components were not the salts but the free substituted diamine and adipic acid. The reaction of polycondensation was run during the initial period in an apparatus provided with a packed column for prevention of volatilization of the diamine [2] at 150-200°. The formula suggested by V. V. Korshak et al.[3] was used for the preliminary calculation of the necessary amount of excess substituted diamine.

The experiments with the preparation of N-substituted polyamides were run with a 10 mole percent excess of the diamine.

In order to prepare the starting polymers, in the synthesis of N-substituted polyamides, for the subsequent treatment with diisocyanate the following diamines were used for the polycondensation reaction with adipic acid: N,N'-di-n-propyl, N,N'-diisopropyl, N,N'-di-n-butyl and N,N'-di-2-butyl-hexamethylenediamines. Some of the properties of the polymers prepared by us are shown in Tables 1 and 2.

TABLE 1

Solubility of N-Alkylated Polyamides Prepared

Polyamide	Solubility					
	H_2O	alcohol	ether	benzene	chloro-benzene	pyridine
N-n-propyl substituted	—	+	—	+	+	+
N-Isopropyl substituted	—	+	—	—	+	+
N-n-Butyl substituted	—	+	—	+	+	+
N-2-Butyl substituted	—	+	—	—	+	+

TABLE 2

Some Properties of the N-Alkylated Polyamides Prepared

Polyamide*	Content of active H per 100 g of the polymer (in mg)	Molecular wt. by end groups**	Viscosity (η)	
			specific, of 3% alcoholic solution	character-istics
N-n-Propyl-substituted	66.5	3000	0.265	0.066
N-Isopropyl-substituted	82.9	2400	0.260	0.060
N-n-Butyl-substituted	55.2	3600	0.398	0.088
N-2-Butyl-substituted	72.0	2800	0.300	0.050

*By Chugaev-Tserevitinov method.

**The alcoholic solution was always basic.

The data in Table 2 make it evident that no significant differences in the magnitudes of molecular weights or characteristic viscosity can be observed among the polyamides with various substituents. The effect of the structure of the substituting radical is manifested in the solubility of the polymers and in the consistency (at normal temperature): polyamides having the normal substituent radical are balsam-like and are readily soluble in benzene, while those with a branched substituent radical are waxy and are insoluble in benzene. The determination of the number of end groups in completely N-alkylated polyamides plays a very significant role since on the basis of the thus obtained values one calculates the amount of the diisocyanate necessary for the lengthening and spatial cross-linking of the polyamide chains.

The determination of the number of end groups was done on the basis of polymer analysis for the content of active hydrogen by the method of Chugaev-Tserevitinov. This method permits one to determine both the secondary amino groups and the carboxyl groups which may exist in small amounts at the chain ends despite the excess amount of the diamine used in the polycondensation reaction.

For running the analysis we used chlorobenzene in the present work, this substance having turned out to be a good solvent for the Chugaev-Tserevitinov reaction. Chlorobenzene dissolves the N-substituted polyamides prepared by us, does not yield gaseous products after the addition of methylmagnesium iodide and has a relatively

TABLE 3

Change of Viscosity of 100%-Substituted Polyamides After Treatment with Diisocyanate

Substituent radical	Specific viscosity of 3% alcoholic solution	
	Starting polymer	Polymer after treatment with diisocyanate
n-Propyl substituted	0.265	0.641
Isopropyl substituted	0.260	0.806
n-Butyl substituted	0.398	1.249
2-Butyl substituted	0.300	0.972

low magnitude of the vapor pressure at the temperature of the determination (6.6 mm at 15°). On the basis of the determination of the number of end groups one may calculate the average numerical molecular weight of the polyamide.

The second stage of the reaction, being considered here, consists, as indicated earlier, of the reaction of the completely N-alkylated polyamides with diisocyanate. 2,4-Toluylenediisocyanate, which had been recommended for similar reactions with polyesters as one of the reactive diisocyanates, was used by us as the agent for chain lengthening of the starting polyamide and for the cross-linking. Initially the chain lengthening of the starting polyamide was run by the addition to the polymer of 2,4-toluylenediisocyanate in an amount calculated at 95 mole % of isocyanate groups per 100 mole % of end groups of the polyamide, followed by heating of the mixture at 130°. The reaction of the isocyanate groups with the NH- or the COOH groups proceeds very rapidly under these conditions, which fact agrees with the literature data on the polyesters. In the present case the reaction rate was controlled by the alteration of viscosity of the polymer solutions. The viscosity of the polymers rose considerably after the addition of the diisocyanate and elevation of the temperature of the reaction mixture to 130°, but the viscosity was almost unaltered on further heating.

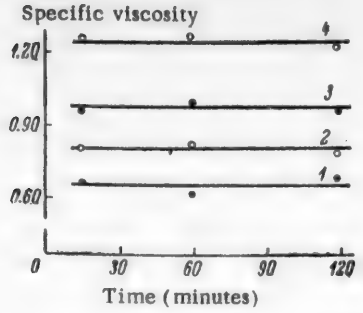
The viscosity of the solutions of N-substituted polyamides after the reaction with diisocyanate rises approximately 2.5-3-fold (see Table 3) which fact indicates the chain lengthening and the corresponding increase of the molecular weight of the polymers. However the polymers retain the ability to dissolve in alcohol and the ability to melt which indicates the absence of tridimensional links in them.

Polyamides with branched substituents at the nitrogen (isopropyl, 2-butyl) form hard brittle polymers as the result of reaction with 2,4-toluylenediisocyanate. Polyamides with normal substituent radicals (n-propyl, n-butyl) form elastic polymers. The observed influence of the radical structure (normal and branched) on the physicomechanical properties of the polyamides agrees with the known data relative to the polyacrylates which are substituted in the chain.

The reaction of spatial interbinding of polyamide chains of the above-indicated structure was realized on an example of the N-isopropyl and N-n-butyl substituted polyamides (after lengthening of their chains by the diisocyanate). The stitching-together (or cross-linking) of the chains was done by prolonged heating (10-12 hours at 150°) of the polymer with additionally added amount of the diisocyanate which reacts with the active hydrogen of the carbamido groups formed in the process of chain lengthening. After the indicated time interval, the polyamides lose the ability to melt and to dissolve (in alcohol), which facts permit us to conclude that a tridimensional structure had formed.

EXPERIMENTAL

The experiments on the preparation of totally N-alkylated polyamides were run in equipment which had been described earlier [2]. Owing to the fact that the polymer formed by this method arises with an excess of the diamine, which locates itself at the chain ends, the preliminary preparation of salts was needless. The reaction mixture was a mixture of adipic acid and the corresponding diamine. For prevention of the loss of the diamine in the nitrogen stream at elevated temperature, the apparatus was provided with a column with a packing for the first stage of the reaction (heating at atmospheric pressure) and the elevation of temperature of the heating bath was done gradually. Heating of the distillate for complete distillation of the resulting water was also switched



Dependence of specific viscosity on the duration of heating of polyamide with diisocyanate.
1) N-n-Propyl substituted; 2) N-isopropyl substituted; 3) N-n-butyl substituted; 4) N-2-butyl substituted.

on after the passage of a certain period of time after the beginning of the reaction. For running the reaction in vacuum the column was replaced by a takeoff tube. The maximum reaction temperature reached 220°. In other respects the reaction was run under the same conditions as in the case of preparation of partially N-alkylated polyamides. The following amounts of components were used for running the polycondensation:

1) 12.1 g of adipic acid and 18.3 g of N,N'-di-n-propylhexamethylenediamine; the resulting polyamide was designated as N-n-propyl substituted.

2) 16.6 g of adipic acid and 25.0 g of N,N'-diisopropylhexamethylenediamine; polyamide notation – N-isopropyl substituted.

3) 14.5 g of adipic acid and 25.0 g of N,N'-di-n-butylhexamethylenediamine; polymer designation – N-n-butyl substituted.

4) 14.5 g of adipic acid and 25.0 g of N,N'-di-2-butylhexamethylenediamine; polymer designation – N-2-butyl substituted.

The excess of the diamine in the starting mixture was 10 mole % in all cases. The reaction time was 20 hours at atmospheric pressure and temperature of 150°, 20 hours at atmospheric pressure and 200°, 10 hours at the pressure of 0.4 mm and 220°. During the reaction the following number of grams of water was distilled in the experiments: 1) 2.9, 2) 3.9, 3) 3.5, and 4) 3.4. The excess diamine which failed to react was also distilled off.

The content of active end groups by the Chugaev-Tserevitinov method was done (the sum of COOH and NHR groups) for the reaction of the completely N-alkylated polyamides with 2,4-toluylenediisocyanate and for the calculation of the necessary amount of the latter for the purpose of chain lengthening in the polymer; the data are given in Table 2.

The reaction of chain lengthening by the diisocyanate was run in a flask with about 70 ml capacity, provided with a stirrer and a reflux condenser, placed in an oil bath. The N-substituted polyamide was placed into the flask and to it there was added the calculated amount of the diisocyanate (95% of isocyanate groups per 100% of polyamide end groups) and the mixture was heated with stirring at 130°. The reaction mixture was maintained at this temperature and after definite time intervals samples were taken from it for the determination of change in viscosity of the polymer (see figure). During the reaction the evolution of gaseous products was observed (CO_2).

For 25.0 g of N-n-propyl substituted polyamide there was taken 1.38 g of 2,4-toluylenediisocyanate; for 30.0 g of N-isopropyl substituted polyamide – 2.06 g of the diisocyanate; for 30 g of N-n-butyl substituted polyamide – 1.37 g of diisocyanate; and for 30.2 g of N-2-butyl substituted polyamide – 1.79 g of diisocyanate.

The reaction of tridimensional linking of the lengthened N-alkylated polyamide chains by means of the diisocyanate at the carbamido groups, which had formed during the chain lengthening of the original polyamide, was run in an air thermostat at 150-155°. The polyamide that had been "lengthened" by the diisocyanate was melted in a porcelain dish, an additional amount of diisocyanate (Table 4) was added to it, the mixture was stirred thoroughly and maintained in the thermostat for a long interval of time. We succeeded in forming a tridimensional structure only after the addition of a considerable excess of the diisocyanate – of the order of 12 weight %. The loss of solubility and the ability to melt in the polymer indicated the formation of the tridimensional structure. The corresponding data are shown in Table 4.

TABLE 4

Data of Experiments on Formation of Cross-Linked Polyamides

Initial polyamide	Amount (in g)	2,4-Toluylene-diisocyanate (g)	Solubility of polymer in alcohol after heating at 150° for period shown (hours)				
			1	3	6	9	12
N-Isopropyl substituted	20.00	2.20	+	+	+	–	–
N-n-Butyl substituted	20.00	2.40	+	+	+	+	–

SUMMARY

1. Completely N-alkylated polyamides were prepared with various substituents; hereby it was shown that polyamides with branched radicals (isopropyl, 2-butyl) have a waxy character, while those with linear radicals (n-propyl, n-butyl) are balsam-like and soluble in benzene.

2. It was established that in the interaction of N-alkylated polyamides with diisocyanate a lengthening of the chains of the former takes place; here the polymers with branched substituents form hard and even brittle products, while those with linear substituents form elastic products.

3. A second treatment with excess diisocyanate leads to the formation of polyamides with tridimensional structure.

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SYNTHESIS OF 2-ETHYL- AND 2-PROPYL-1,3-BUTADIENES

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and M. F. Egudina

The literature on the synthesis of β-substituted diene hydrocarbons is a rather limited [1, 2]. The most acceptable amount of described methods of synthesis are those based on pyrolysis of the corresponding acetates [3-5]. The method of preparation of β-alkylbutadienes, proposed by Carothers [6], from α-chloromethylallene and alkylmagnesium halides was not used owing to the difficulty of preparation of the α-chloromethylallene.

It was shown in our laboratory that during the continuous running of the process of hydrochlorination of vinylacetylene in the presence of cuprous chloride under certain conditions it is possible to obtain up to 50% of α-chloromethylallene, along with chloroprene [7]. This fact led us to undertake anew a study of synthesis of butadienes from α-chloromethylallene. We prepared 2-ethyl- and 2-propyl-1,3-butadienes by the action of corresponding alkylmagnesium halides on this substance. The yield of alkylbutadienes did not rise above 26% under the conditions explored by us, this being caused by a number of side reactions.

From the by-products of the reaction there were isolated: the dimer of propyl-1,3-butadiene, n-hexane and 1,3-hexadiene. The formation of the latter may be explained by replacement of chlorine by an alkyl group in α-chloromethylallene with the subsequent isomerization of the resulting allenic compound into the diene.

In addition, in all cases there was obtained a considerable amount of polymers which was evidently connected with the possibility of a condensation of two molecules of α-chloromethylallene with formation of octatetraene (with allenic structure) and subsequent isomerization of it into a compound with a conjugated double bond system, which compound polymerized under the experimental conditions used.

$$CH_2=C=CH-CH_2-CH_2-CH=C=CH_2 \rightarrow CH_2=CH-CH=CH-CH=CH-CH=CH_2$$

The properties of the alkylbutadienes prepared by us are given in the table. The unsaturation of the hydrocarbons was determined by the titration with bromine according to Kaufman, by bromide-bromate and bromo-iodine methods. The best results were obtained with the Kaufman solution, but even in this case the addition of bromine proceeded very slowly, so that for complete reaction the sample must stand for 2-3 days. Thus, for example, the unsaturation of ethylbutadiene as determined by standing for one day was 80%, after two days it was 94%, after three days it was 97% and after seven days it was 97%.

For proof of the diene structure the alkylbutadienes were condensed with maleic anhydride in benzene solution. The reaction proceeded very violently and began immediately on mixing the benzene solutions of alkylbutadiene and maleic anhydride. The melting points of the products thus prepared are shown in the table.

EXPERIMENTAL

The preparation of α-chloromethylallene was described by us earlier [7, 8].

The synthesis of 2-ethylbutadiene was carried out in the following fashion. To an ethereal solution of the organomagnesium compound, prepared from magnesium shavings and ethyl chloride in a three-liter flask with four necks, there was added, with energetic stirring, the α-chloromethylallene at such a rate that the reaction temperature failed to rise over 40°. The organomagnesium compound was taken in 10% excess relative to the α-chloromethylallene. After the addition of the entire amount of α-chloromethylallene, the agitation of the thick reaction

Properties of Alkylbutadienes

Substance	Boiling point	d_4^{20}	n_D^{20}	Molecular weight (cryoscopic)		MR_D		M.p. of adduct with maleic anhydride		Carbon (in %)		Hydrogen (in %)		Remarks
				found	calc.	found	calc.	before hydrolysis	after hydrolysis	found	calc.	found	calc.	
2-Ethyl-1,3-butadiene	65—66°	0.7197	1.4328	81.60	82.14	29.62	28.97	67—68°	140°	87.94	87.73	12.10	12.27	Our data
	66	—	1.4325	—	82.14	—	28.97	67—69	—	—	—	—	—	[4]
	66.6	0.7154	1.4328	—	82.14	29.76	28.97	—	—	—	—	—	—	[9]
2-Propyl-1,3-butadiene*	92—93	0.7313	1.4361	96.30	96.16	34.33	33.59	47—48.5	161	87.08	87.43	12.70	12.57	Our data

*2-Propyl-1,3-butadiene had not been described in the literature.

mixture was continued for 2-3 hours, after which the decomposition of the excess organomagnesium compound and the formed complex was done by means of a cooled saturated solution of ammonium chloride and 5% hydrochloric acid. The ethereal layer was separated, washed with cooled saturated solution of ammonium chloride and dried over calcined magnesium sulfate. After the removal of ether, the reaction products were distilled in vacuum and then were distilled twice through an effective column with a Nichrome packing.

The working-up of the reaction products was done as follows in one of the first experiments. After completion of the reaction and the layering-out of the ether, the latter was separated from the crystalline residue. The residue was washed with absolute ether and the ethereal solutions were combined (first ethereal extract). Then the crystalline residue was treated with a cooled saturated solution of ammonium chloride. Heat evolution was observed and part of the crystalline residue dissolved. The oily layer which formed thereby was separated. Organic substances were extracted with ether from the aqueous layer along with the crystalline residue and the ethereal extract was added to the oily layer (second ethereal extract). Then, the aqueous solution with the precipitate was treated with 5-10% hydrochloric acid until the precipitate dissolved. The organic matter was extracted from the acidic aqueous solution with ether (third ethereal extract). All the ethereal extracts were dried with calcined magnesium sulfate, after which each extract was worked up separately; the ether was distilled off and the organic residue was subjected to fractionation. As the result of such treatment it was shown that no organic residue was contained in the third ethereal extract, while the first and the second extracts contained approximately equal (by weight) amounts of organic products, the composition of which was almost the same. Thus one may conclude that in the process of the reaction there is formed a complex which decomposes partially even prior to the addition of the aqueous solution of ammonium chloride. Starting with this conclusion, the above separate working-up of the condensation products was not used in the subsequent experiments.

Two fractions were isolated from the by-products in the synthesis of ethylbutadiene:

1st: b.p. 73-75°, d^{20}_4 0.7495, $n^{20}D$ 1.4190, M 81.12;
2nd: b.p. 43-45° (20 mm), d^{20}_4 0.8308, $n^{20}D$ 1.4370, M 125.7.

Found %: C 76.46, 76.30; H 10.85, 11.03; Cl 5.46.

The first fraction was obtained in negligible amounts when the reaction was run in diethyl ether and was the principal fraction when the reaction was run in dibutyl ether.

It was established that this fraction contains about 50% of 1,3-hexadiene (by test reaction with maleic anhydride), a certain amount of carbonyl compounds the structures of which were not determined, and about 5% of α-chloromethylallene (by content of hydrolyzable chlorine).

The certain discrepancy of the constants of the first fraction with the literature data on 1,3-hexadiene is evidently explained by the presence of admixed carbonyl compounds of α-chloromethylallene.

The second fraction contains about 50% of dienic compound and in it, according to infrared spectroscopic data, there is a certain amount of allenic compounds (infrared spectrum shows the 5.09 μ band). One may suppose that the hydrocarbon contained in the second fraction is the above-mentioned octatetraene with admixture of other compounds whose composition was not determined. The formation of butane (from ethyl bromide by the Wurtz reaction) was not observed at all.

From the by-products in the synthesis of propylbutadiene, which was carried out under the same conditions as the synthesis of ethylbutadiene, there were isolated: (b.p. 68°, d^{20}_4 0.656, $n^{20}D$ 1.3760) and the dimer of propylbutadiene.

B.p. 93° (4 mm), d^{20}_4 0.8537, $n^{20}D$ 1.4751, MR_D 63.38; calculated 63.72.
Found: M 191.65. $C_{14}H_{24}$. Calculated: M 192.33.

SUMMARY

1. 2-Ethyl and 2-propyl-1,3-butadienes were synthesized by the action of corresponding organomagnesium compounds on α-chloromethylallene. The latter product is being described for the first time.

2. A dimer of 2-propyl-1,3-butadiene was isolated from the by-products of the synthesis of propylbutadiene and suitably characterized.

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HOMOLOGS OF MONOVINYLACETYLENE

VII. DEHYDRATION OF SECONDARY ACETYLENIC ALCOHOLS

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Hydrocarbons of the vinylacetylene series with alkyl substituents at the terminal carbon atoms of the conjugated system may be prepared by dehydration of secondary acetylenic alcohols. Such vinylacetylenic hydrocarbons have been of interest to us from the point of view of a study of their styrene-type dimerization [1].

The dehydration of four secondary acetylenic alcohols: isopropylethynylcarbinol (I), n-propylethynylcarbinol (II), isopropyl (methylethynyl)-carbinol (III) and ethyl(methylethynyl)carbinol (IV), was studied in the present investigation.

$(CH_3)_2CH-CHOH-C\equiv CH$ (I) $\quad CH_3CH_2CH_2CHOH-C\equiv CH$ (II)

$(CH_3)_2CH-CHOH-C\equiv C-CH_3$ (III) $\xrightarrow[325^\circ]{Al_2O_3}$ $(CH_3)_2C=CH-C\equiv C-CH_3$ (V)

$CH_3CH_2CHOH-C\equiv C-CH_3$ (IV) $\xrightarrow[270^\circ]{MgSO_4}$ $CH_3CH=CH-C\equiv C-CH_3$ (VI)

Alcohols (I) and (II) were prepared by us according to A. E. Favorskii's method in yields of 60-65%. The condensation of aldehydes with acetylene according to the A. E. Favorskii's method may be realized in good yields under the conditions of slow addition of greatly diluted ethereal solution of the aldehyde to the reaction mixture.

The aldehyde may react in two directions under the conditions of the Favorskii reaction:

$$R-C\begin{matrix}O\\H\end{matrix} + KC\equiv CH \rightarrow RCH(OK)\equiv CH \qquad (1)$$

$$R-C\begin{matrix}O\\H\end{matrix} \xrightarrow{KOH} \text{aldol condensation} \qquad (2)$$

If the rate of the first condensation reaction is sufficiently great, then owing to the absence of excess aldehyde in the reaction mixture, the aldol condensation does not take place.

We set up a large number of experiments on dehydration of secondary acetylenic alcohols—isopropylethynylcarbinol (I) and n-propylethynylcarbinol (II). In catalytic dehydration over Al_2O_3, $NH_4H_2PO_4$ on carbon and pumice, unfired porcelain and $MgSO_4$ at 250-300° the alcohols (I) and (II) were mainly recovered unchanged. Raising the temperature of dehydration to 320° also failed to lead to even traces of hydrocarbons. Therefore it was evident that secondary α,β-acetylenic alcohols with a terminal acetylenic group, (I) and (II) do not lose water under conditions which are usual for catalytic dehydration of tertiary α,β-acetylenic alcohols.

We also attempted to realize the transition from alcohol (I) to the hydrocarbon, 2-methyl-2-penten-4-yne, through the ester of p-toluene-sulfonic acid [2], but the reaction of decomposition of the sulfonate led to formation of resinification products or, in the case of decomposition by means of sodium alcoholate, to the formation

of a mixture of substances containing an ethoxyl group. The starting materials for the synthesis of hydrocarbons with substituents at both ends of the conjugated system – 2-methyl-2-hexen-4-yne (V) and 2-hexen-4-yne (VI), were the corresponding secondary acetylenic alcohols – isopropyl (methylethynyl)-carbinol (III) and ethyl(methylethynyl)carbinol (IV). In running the synthesis of these alcohols by the Iotsich method it was established that the yield of the alcohols is raised if the reaction mixture, after the addition of the aldehyde, is heated on a water bath for 4-5 hours and is left to stand for 5-6 days.

Vinylacetylenic hydrocarbons: 2-methyl-2-hexen-4-yne (V) and 2-hexen-4-yne (VI) were prepared by dehydration of these alcohols (III) and (IV). These hydrocarbons fit, respectively, the formulas C_7H_{10} and C_6H_8 in their elemental composition and molecular weight. The hydrocarbons added to the theoretical amount of hydrogen, calculated for one double and one triple bond, during catalytic hydrogenation over platinum black.

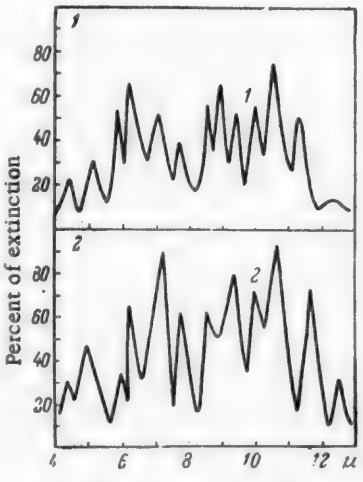
Physical Properties of Hydrocarbons (V) and (VI)

Hydrocarbon	d_4^{20}	n_4^{20}	n_F^{20}	n_C^{20}	MR_D found	MR_D calc.	ME_D	$\omega_{F,C,D}$
(V)	0.7849	1.46595	1.47684	1.46232	33.21	32.06	1.15	31.16
(VI)	0.7703	1.46339	1.47431	1.45926	28.67	27.44	1.23	32.47

Exaltation of molar refraction is equal to one unit on the average [3, 4] in the series of vinylacetylenic hydrocarbons of type:

$$R-CH=CH-C\equiv C-R$$

The magnitude of relative dispersion also permits us to draw the conclusion about the presence in hydrocarbons (V) and (VI) of a system of conjugated bonds [5]. The structure of hydrocarbon C_7H_{10} (V) was proved by the way of oxidation and ozonolysis.



Infrared absorption spectra of 2-hexen-4-yne (1) and 2-methyl-2-hexen-4-yne (2).

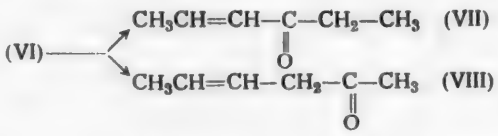
As the result of the oxidation there were isolated acetone, acetic and oxalic acids. The absence of the possible isomerization product with a terminal methylene group was established by ozonolysis of hydrocarbon (V) [9]. These data permitted us to assign the structure of 2-methyl-2-hexen-4-yne to hydrocarbon (V). The chemical proof of structure was confirmed spectroscopically by taking the spectrum in the infrared region (see figure). On the basis of refractometric data and the infrared spectrum (see figure) the structure of a conjugated vinylacetylenic hydrocarbon – 2-hexen-4-yne, was assigned to hydrocarbon C_6H_8 (VI).

It is evident in the examination of the infrared spectra of the hydrocarbons under study that both hydrocarbons are substituted vinylacetylenic hydrocarbons: the absorption bands which correspond to the bond vibrations of the double and the doubly substituted triple bonds are somewhat shifted from their normal positions owing to the conjugation (V) 1613 cm^{-1}, 2270 cm^{-1}, and (VI) 1607 cm^{-1}, 2270 cm^{-1} [6, 7]. The structure of hydrocarbon (V) as that of an enyne hydrocarbon containing a triply substituted double bond is confirmed by the following data: the deformational nonplanar vibrations of the C–H bond in the system $RCH=CRR_2$ (trisubstituted ethylene) are characterized by absorption in the region of 800-840 cm^{-1} [8]. A frequency of 856 cm^{-1} was found in the spectrum [9] of the enyne hydrocarbon – 3,5-dimethyl-3-hexen-1-yne, at the infrared region. A frequency of 859 cm^{-1} was discovered in the spectrum of hydrocarbon (V). Hydrocarbon (V) does not contain any admixture of the isomer with a terminal methylene group, since the frequencies 903 and

1410 cm^{-1} are absent from its spectrum [6, 9]. This conclusion coincides completely with the ozonolysis data.

The infrared spectrum of hydrocarbon (VI) is not discussed in detail in this paper since the separation of it into cis and trans isomers was not performed by us.

The reaction of hydration was studied for hydrocarbon C_6H_8 (VI). As it is known, vinylacetylenic hydrocarbons with a terminal acetylenic group always add water in accord with the Markovnikov rule with formation of the acetyl grouping. In case of hydrocarbon (VI), on the basis of electronic concepts, one may expect the formation of a mixture of ketones: 4-hexen-3-one (VII) and 4-hexen-5-one (VIII).



It was shown during the examination of the hydration products that the main reaction product is a ketone with a conjugated system of bonds (VII). This conclusion was drawn on the basis of examination of the absorption curve in the ultraviolet region of the spectrum, since the molar extinction coefficient at the short wave maximum coincided with the literature data for α,β-unsaturated ketones [10].

EXPERIMENTAL

Synthesis of isopropylethynylcarbinol (I). Into a three necked flask provided with a propeller stirrer, a reflux condenser and a dropping funnel there was placed 150 g of powdered potassium hydroxide and 500 ml of absolute ether. A strong stream of acetylene was passed into the ether, with snow cooling, for thirty minutes. To the acetylene-saturated solution (with uninterrupted stream of acetylene) there was added over ten hours drop by drop a solution of 20 g of isobutyraldehyde in 400 ml of absolute ether. The alcoholate was decomposed on the following day by 200 ml of water. The ethereal layer was separated, washed with 2% acetic acid and water. The ethereal layer was dried for one day over calcined potassium carbonate.

B.p. 51° (30 mm), $n^{20}D$ 1.4369, d^{20}_4 0.9291 [11, 12]. $C_6H_{10}F$. Calculated MR_D 29.43. Found MR_D 20.09.

The yield of isopropylethynylcarbinol was 60-65%.

Synthesis of the sulfonate of isopropylethynylcarbinol. To 23.6 g of p-toluenesulfonyl chloride in 12 ml of pyridine there was added dropwise with energetic stirring 11 g of carbinol (I). After completion of the addition of the carbinol the reaction mixture was allowed to stand for 18 hours. After cooling and continued stirring, 15 ml of water was added to the flask, after which the reaction mixture was poured into water. The sulfonate was extracted with ether. The ethereal extract was washed twice with 10% sulfuric acid, with a sodium carbonate solution and with water. The ethereal solution was then dried over sodium sulfate. After the distillation of ether, the sulfonate precipitated in the form of colorless crystals. M.p. 32.5° (from alcohol).

Found %: S 12.09, 12.09. M 260.3. $C_{13}H_{16}O_3S$. Calculated %: S 12.26. M 252.3.

The synthesis of n-propylethynylcarbinol (II) was run under conditions given for the synthesis of isopropylethynylcarbinol. The yield of the carbinol was 60%.

B. p. 87-88° (100 mm), $n^{20}D$ 1.4350, d^{20}_4 0.8710 [11, 12]. MR_D 2935. $C_6H_{12}OF$. Calculated 29.43.

Synthesis of isopropyl(methylethynyl)carbinol (III). To 17 g of magnesium shavings covered with absolute ether there was added dropwise a solution of ethyl bromide (72 g) in double volume of ether. The resulting ethylmagnesium bromide was diluted with a large volume of ether (about 800 ml). Methylacetylene was introduced in 1.5-fold excess, over the calculated amount, into the reaction mixture with ice cooling and energetic stirring. After the reaction mixture had separated into layers, isobutyraldehyde (30 g) was added to the flask. The reaction products were heated at 40° on a water bath and then were allowed to stand for 5-6 days. The organomagnesium complex was carefully decomposed at first with water (50 ml), then with 10% hydrochloric acid. The ethereal solution was neutralized with 10% solution of sodium carbonate, washed with water and dried with potassium carbonate. The yield of the carbinol was 87%.

B.p. 99° (90 mm) [13], $n^{20}D$ 1.4510, d^{20}_4 0.8860, MR_D 34.09. $C_7H_{12}O$F, Calculated 34.05.

Hydrogenation of carbinol (III) was conducted in the presence of platinum black. Carbinol sample: 0.8 g in 25 ml of ethyl alcohol; Pt: 0.08 g. There was absorbed 337.2 ml of hydrogen (0°, 760 mm); the theoretical amount was 320 ml.

Synthesis of ethyl(methylethynyl)carbinol (IV) was run under the conditions which were indicated for the synthesis of carbinol (III).

B.p. 93-94° (90 mm), $n^{20}D$ 1.4508, d^{20}_4 0.8963, MR_D 29.48. $C_6H_{10}O$. Calculated 29.43.
Found %: C 73.10, 73.35; H 10.35; M 98.75. $C_6H_{10}O$. Calculated %: C 73.42; H 10.27; M 88.14.

Hydrogenation of carbinol (IV) was run in the presence of platinum black. Carbinol sample: 1 g in 25 ml of ethyl alcohol; Pt: 0.1 g. There was absorbed 464.1 ml of hydrogen (0°, 760 mm); theoretical amount: 457.1 ml.

Dehydration of isopropyl(methylethynyl)carbinol. Twenty grams of isopropyl(methylethynyl)carbinol was passed over ten hours in carbon dioxide atmosphere through a tube filled with unglazed porcelain at 300°. The reaction products were collected in a receiver cooled with ice. The hydrocarbon layer was dried with potassium carbonate and distilled in vacuum through a column in a stream of carbon dioxide. There were obtained the following fractions: 1st, b.p. 50-54° (90 mm), 1.4 g, $n^{20}D$ 1.4570; 2nd, b.p. 55-56.5° (90 mm), 4.9 g, $n^{20}D$ 1.4632; 3rd, b.p. 74-79° (90 mm), 6.5 g, $n^{20}D$ 1.4485 (carbinol).

The second fraction corresponds to hydrocarbon (V). The yield of the hydrocarbon was 44%.

Investigation of hydrocarbon (V) C_7H_{10}. After second vacuum distillation in carbon dioxide atmosphere the hydrocarbon boiled at 56-57° (90 mm) (see table).

Found %: C 89.55, 89.38; H 10.77, 10.88; M 94.1. C_7H_{10}. Calculated %: C 89.29; H 10.70; M 94.15.

Hydrogenation of hydrocarbon (V) was run catalytically in the presence of platinum black. The hydrocarbon sample: 0.8 g in 25 ml of ethyl alcohol; Pt: 0.08 g. There was absorbed 581.8 ml (0°, 760 mm) of hydrogen. The theoretical amount was 571.9 ml.

Oxidation of hydrocarbon (V). To 1.5 g of the hydrocarbon in 100 ml of water there was added, with cooling to 0° and vigorous shaking (the oxidation was run in a flask with a ground-in stopper), crystalline potassium permanganate in small portions until cessation of decolorization. In all 8.4 g of potassium permanganate was added, instead of 9.4 g required theoretically. After completion of addition of potassium permanganate, the manganese dioxide was filtered off, washed on the filter with hot water and the neutral products were distilled from the filtrate. The distillate was utilized for the preparation of p-nitrophenylhydrazone while acetone was determined quantitatively in a separate portion by the hydroxylamine method. The p-nitrophenylhydrazone, recrystallized from alcohol, melted at 148° and gave no depression in mixture with the p-nitrophenylhydrazone of acetone. It was established by oximation that 10 ml of the aliquot sample contained 0.04 g of acetone. On recalculation to the entire solution, the acetone content in the oxidation products was found to be 0.4 g (44%).

The volatile acids were distilled from the acidified solution of the salts. The acids were titrated with 0.1 N solution of sodium hydroxide; 120 ml of 0.1 N sodium hydroxide was required for the titration, which amount corresponded to 0.72 g (75%) of acid, as calculated in terms of acetic acid. The solution of the salts of volatile acids after the neutralization was concentrated to a volume of 40-50 ml. After acidification the acids were distilled into a flask with freshly prepared silver carbonate. The resulting silver salts corresponded to the silver salt of acetic acid in their composition.

Found %: C 14.61, 14.58; H 2.12, 2.08; Ag 65.04, 64.91. $C_2H_3O_2Ag$. Calculated %: C 14.36; H 1.94; Ag 64.66.

The nonvolatile acids were extracted in an extractor. Oxalic acid (m.p. 102°) was isolated in an insignificant amount. The acid was identified by mixed melting point with an authentic specimen.

Ozonolysis of hydrocarbon (V). The ozonolysis was run for the quantitative determination of formaldehyde and formic acid. If the hydrocarbon had contained a considerable admixture of the isomeric hydrocarbon with a terminal methylene group, the ozonolysis products should have contained formaldehyde and formic acid. The

ozonolysis was run in chloroform in A. I. Iakubchik's apparatus. The amount of formaldehyde, determined through formaldehyde derivative of dimethylcyclohexanedione, was 0.47% (calculated for the ozonide). The amount of formic acid (determined by the calomel method) was 1.1% (calculated on the ozonide). Such insignificant amounts of formaldehyde and formic acid are always contained in ozonolysis products; therefore the hydrocarbon (V) does not contain the admixture of a hydrocarbon with a terminal methylene group.

The spectrum in the infrared region was determined for the hydrocarbon (V) on the IKS-11 spectrometer. The layer thickness was 0.05 mm; sodium chloride prism was used (see figure).

Dehydration of ethyl(methylethynyl)carbinol. Forty grams of ethyl(methylethynyl)carbinol was passed over 15 hours through a tube filled with magnesium sulfate at 270°. The dehydration was run in an atmosphere of nitrogen. The reaction products were collected in a receiver cooled with ice. The hydrocarbon layer was dried with potassium carbonate and distilled in vacuum in nitrogen atmosphere. There were collected the following fractions: 1st, b.p. 18-35° (90 mm), 0.8 g, $n^{20}D$ 1.4570; 2nd, b.p. 35.5-36.5° (90 mm), 9.2 g, $n^{20}D$ 1.4630 (hydrocarbon); 3rd, b.p. 38-40° (90 mm), 0.9 g, $n^{20}D$ 1.4580; 4th, b.p. 83-92° (90 mm), 14.5 g, $n^{20}D$ 1.4505 (carbinol). The yield of the hydrocarbon fraction was 44% based on the reacted carbinol.

Investigation of hydrocarbon C_6H_8 (VI). After second distillation in vacuum in nitrogen atmosphere the hydrocarbon had the following properties: b.p. 91-92° (760 mm), 35.5-36.5° (90 mm) (see table).

Found %: C 89.76, 89.62; H 10.17, 10.16. M 79.4. C_6H_8. Calculated %: C 89.95; H 10.06; M 80.13.

The spectrum of hydrocarbon (VI) was determined in the infrared region by means of IKS-11 spectrometer. Lithium fluoride and sodium chloride prisms were used. The layer thickness was 0.05 mm (see figure).

Hydrogenation of hydrocarbon (VI) was run catalytically in the presence of platinum black. The hydrocarbon sample: 1.0 g; Pt: 0.7 g. There was absorbed 840.0 ml of hydrogen (0°, 760 mm); theoretical amount was 839.7 ml.

Hydration of hydrocarbon C_6H_8 (VI). Into a three-necked flask, provided with a stirrer, a reflux condenser, thermometer and a dropping funnel, there was placed 180 ml of water, 7 ml of concentrated sulfuric acid, 3 g of mercuric oxide and 10 ml of 50% solution of $Fe_2(SO_4)_3$. The reaction mixture was heated to 70°, after which 9 g of the hydrocarbon was added to it dropwise. After the addition of the hydrocarbon, the reaction mixture was heated for two and a half hours longer at 70-75°.

The ketone was distilled in vacuum in nitrogen atmosphere. There were obtained the following fractions: 1st, b.p. 69° (90 mm), 0.3 g, $n^{20}D$ 1.4368; 2nd, b.p. 74.5-76.5° (90 mm), 4.7 g, $n^{20}D$ 1.4386 (ketone); flask residue: 0.5 g. The yield of the ketone fraction was 48%.

Investigation of the second fraction.

B.p. 74.5-76.5° (90 mm), $n^{20}D$ 1.4386, d^{20}_4 0.8580 [14]; MR_D 30.12. $C_6H_{10}O$. Calculated 29.45.
Found %: C 73.24, 73.48; H 10.58, 10.61. C_6H_{10}. Calculated %: C 73.42; H 10.27.

The absorption curve was taken for this fraction, by means of the SF-4 spectrophotometer. Ethyl alcohol was used as the solvent (c = 0.00466-0.00003 ml). Wavelength of absorption maximum was 224 mμ, log ε 4.13; another maximum at 310 mμ, log ε 1.57.

2,4-Dinitrophenylhydrazone was prepared from the ketone. The hydrazone thus prepared was red and contained an insignificant admixture of yellow crystals. M.p. 95-106°.

Found %: N 20.24, 20.39. $C_{12}H_{14}O_4N_4$. Calculated %: 20.13.

SUMMARY

1. A method of synthesis of secondary acetylenic alcohols by the A. E. Favorskii method was worked out.

2. It was shown that secondary α,β-acetylenic alcohols with a terminal acetylenic group do not lose water under conditions which are usual for the dehydration of tertiary α,β-acetylenic alcohols.

3. There were prepared and characterized two enyne hydrocarbons: 2-methyl-2-hexen-4-yne and 2-hexen-4-yne, which were obtained by the dehydration of isopropyl(methylethynyl)carbinol and the ethyl (methylethynyl) carbinol which was synthesized for the first time.

4. It was shown spectroscopically that hydration of 2-hexen-4-yne leads mainly to the formation of the α,β-unsaturated ketone 4-hexen-3-one.

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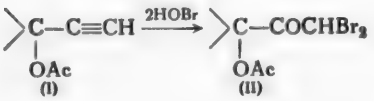
THE SIMPLEST ANALOGS OF CORTICOSTEROIDS

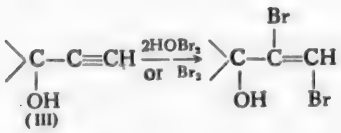
II. INTRODUCTION OF DIHYDROXYCARBOXYLIC, GLYCERYL AND HYDROXYACETONE SIDE CHAINS INTO o-METHYLCYCLOHEXANONE AND THE STEREOCHEMISTRY OF THE COMPOUNDS FORMED THEREBY

I. N. Nazarov and A. A. Akhrem

Introduction of the dihydroxyacetone side chain into cyclic compounds is of considerable interest in connection with the problem of the total synthesis of cortisone and its simplest analogs. The absence of satisfactory methods of introduction of the dihydroxyacetone side chain into steroidal ketones forces organic chemists to seek some new paths to the solution of this important problem. Several years ago we used for this purpose [1] the reaction of addition of hypobromous acid to the triple bond, reaction discovered by Favorskii [2], with its employment among the readily preparable acetylenic alcohols and their acetates.

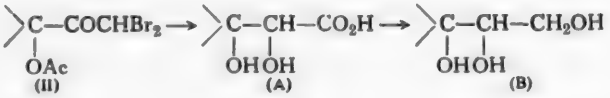
As it turned out in the case of acetates of tertiary acetylenic alcohols (I), the reaction of addition of hypobromous acid to the triple bond proceeded normally and led to the preparation of the corresponding acetates of the dibromoketols (II), while in the case of alcohols (III) there occurred the addition of two atoms of bromine to the triple bond.





The same regularity is observed in the case of addition of hypobromous acid to the vinyl analogs of compounds (I) and (III).

We observed an intramolecular rearrangement during the reaction of barium hydroxide with the acetates of dibromoketols (II), this rearrangement leading to the formation of the corresponding dihydroxycarboxylic acids (A) which may be reduced with lithium aluminum hydride to the corresponding triols (B), which are important intermediates in the synthesis of the dihydroxyacetone side chain.

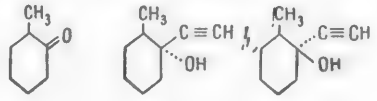


The absence of asymmetric centers in the acetylenic alcohols, previously described by us [1], did not permit us to study the stereochemistry of these interesting reactions.

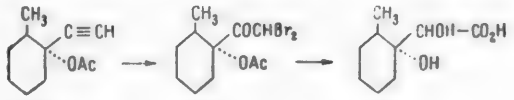
We selected the accessible o-methylcyclohexanone (IV), in the molecule of which there exists one asymmetric center, for the simplest model compound with which one may study the stereochemistry of the introduction of a side chain into cyclic compounds.

The results of our studies are presented in this communication.

Two epimeric acetylenic alcohols: crystalline (V) and liquid (VI), are formed in the condensation of o-methylcyclohexanone (IV) with acetylene under pressure [3] in the presence of powdered potassium hydroxide. Here the quantitative ratio of the epimers (V) and (VI) depend, evidently, on the conditions used for the experiment. Thus, in the synthesis run in liquid ammonia [4] there is formed 33% of (V) and 66% of (VI), while under the Favorskii reaction conditions the yield of the crystalline isomer (V) reaches 60%. The formation of two epimers (V) and (VI) has been observed previously [5], but only rather recently [4] were these isolated in the pure state. However, their geometric configuration has not been determined until the present. Recently we [6] related the epimeric acetylenic alcohols (V) and (VI) to the known pair of cis- and trans-1,2-dimethylcyclohexanols [7], and thereby showed that the crystalline 1-ethynyl-2-methylcyclohexanol (V) corresponds to the cis-disposition of the methyl and the ethynyl groups, while the liquid epimer (VI) corresponds to the trans-disposition of these groups. This result is also confirmed by the data obtained previously [8] on the behavior of dienes synthesized from epimeric alcohols (V) and (VI) in the reaction of diene synthesis.

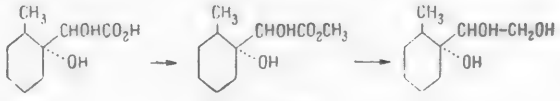


The acetate of cis-1-ethynyl-2-methylcyclohexanol (VII) was prepared in high yield during the acetylation of alcohol (V) by excess acetic anhydride. By the action of hypobromous acid on the latter there is obtained, in 95% yield, the crystalline acetate of cis-1(ω-dibromoacetyl)-2-methylcyclohexanol (VIII).



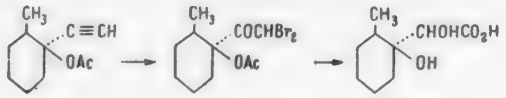
The intramolecular rearrangement, described by us earlier [1], takes place during the action of an aqueous solution of barium hydroxide on the acetate of the cis-dibromoketol (VIII), and during this reaction there is formed, in yield of about 50%, the mixture of the two isomeric dihydroxycarboxylic acids (IX) and (X), with melting points 149-150° and 128.5-129°, respectively, which are predicted by theory and which differ from each other in the configuration of the secondary hydroxyl.

The acid (IX) is formed in greatly predominant amount. Its methyl ester (XI) is formed by the action of an ethereal solution of diazomethane on acid (IX) and the reduction of this ester with lithium aluminum hydride led to the formation, in high yield, of the triol (XII) with melting point 88-88.5°.



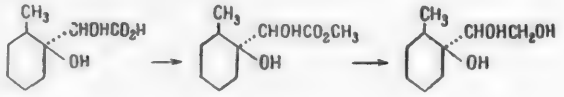
Acid (X) gave, under these conditions, a crystalline methyl ester (XIII) with m.p. 73-74° on the reduction of which with lithium aluminum hydride there was formed, in 50% yield, the triol (XIV), with m.p. 90-90.5°, which was epimeric to triol (XII) at the secondary hydroxyl group. The mixed melting point of the isomeric triols (XII) and (XIV) shows a large depression and melts at 50-55°.

Analogous transformations were also realized with the liquid transacetylenic alcohols (VI). Its acetate (XV) was prepared by acetylation of the latter, and, by the action of hypobromous acid on this acetate, there was formed in 95% yield the acetate of trans-1(ω-dibromoacetyl)-2-methyl-cyclohexanol (XVI).



(XV) (XVI) Liquid (XVII) (XVIII)

The intramolecular rearrangement, which leads to the formation, in 50% yield, of a second pair of dihydroxy-carboxylic acids (XVII) and (XVIII), with melting points 156-156.5° and 109.5-110°, respectively, which are epimeric at the secondary hydroxyl, again takes place during the hydrolysis of the acetate of the dibromoketol (XVI) with barium hydroxide. Again in this case the high-melting acid (XVII) was isolated in the predominant amount. Thus, the intramolecular rearrangement of the acetate of dibromoketols (VIII) and (XVI) does not proceed stereospecifically. The methyl ester (XIX), with m.p. 91-91.5°, of the high-melting acid (XVII) was prepared by the action of an ethereal solution of diazomethane on the acid; the reduction of this ester with lithium aluminum hydride gave the triol (XX), with m.p. 125-125.5°, in high yield.



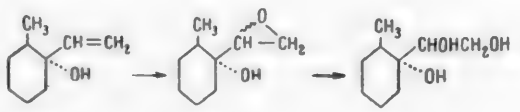
(XVII) (XVIII) (XIX) (XXI) (XX) (XXII)

Trans-acid (XVIII) under these conditions gave its methyl ester (XXI) with m.p. 53-54°, on the reduction of which with lithium aluminum hydride there was obtained triol (XXII), with m.p. 88-88.5°, in 50% yield. The reaction gave directly a triol with m.p. 76-78° (from ether) and a small amount of crystals with m.p. 88-88.5°. Its mixed melting point with a sample of XII), which also melts at 88-88.5°, gave m.p. 55-65°.

Attempts to prepare acetonates of the dihydroxy acids (IX) and (XVII) turned out to be fruitless.

The triols (XII), (XIV), (XX) and (XXII), described above,are important intermediates in the synthesis of the dihydroxyacetone side chain. For their preparation we also used the glycidic method described by us previously [1].

Selective catalytic hydrogenation of the cis-acetylenic alcohol (V) over palladium catalyst gave, in high yield, the cis-1-vinyl-2-methyl-cyclohexanol (XXIII), the oxidation of which with peracetic acid, by the Prilezhaev method, in chloroform gave 80% yield of a mixture of isomeric glycidic alcohols (XXIV) in the form of crystals and a liquid oil.

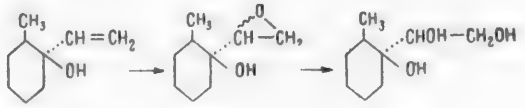


(XXIII) (XXIV) (XII) (XIV)

The crystalline glycidol (XXIV), formed in the greater amount, is hydrolyzed, on heating with acidified water, to triol (XII), in good yields, this triol having been also obtained, as indicated above, from the high-melting isomer of the cis-acid (IX), which was also formed in a predominant amount.

The liquid glycidol (XXIV) gave on hydrolysis a certain amount of a difficultly crystallizable thick sirup from which there was isolated a small amount of crystals of triol (XIV) which did not give a mixed melting point depression with the specimen, described above, which was prepared by reduction of acid (X). On selective

hydrogenation of trans-1-ethynyl-2-methylcyclohexanol (VI) there was formed trans-1-vinyl-2-methylcyclohexanol (XXV), the oxidation of which with peracetic acid led to the preparation of glycidic alcohols (XXVI), isolated in the form of two crystalline isomers with m.p. 41° and 75°. The high-melting isomer was isolated in the predominant amount.



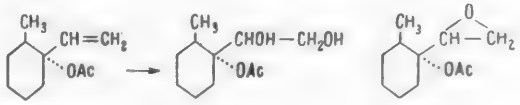
(XXV) (XXVI) (XX) (XXVII)

Hydrolysis of the low-melting isomer (XXVI) gave the triol (XXII), with m.p. 88.5°, synthesized by us by the reduction of the low-melting acid (XVIII). The above-described triol (XX), synthesized by the reduction of the high-melting acid (XVII), was obtained on hydrolysis of the high-melting glycidol (XXVI).

As it is evident from the experimental results, the oxidation of vinyl alcohols (XXIII) and (XXV) with peracetic acid proceeds unselectively and leads to the formation of all possible isomers of the glycidic alcohols (XXIV) and (XXVI) with different configurations of the oxide ring.

In the selective catalytic hydrogenation over palladium catalyst of the cis-acetate (VII) there was formed the acetate of cis-2-methyl-1-vinyl-1-cyclohexanol (XXVIII); the trans-acetate (XV), under these conditions, gave the acetate of trans-2-methyl-1-vinyl-1-cyclohexanol (XXIX).

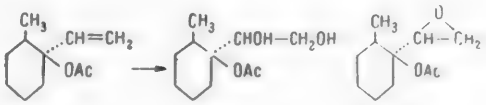
In oxidation of the acetate (XXVIII) with peracetic acid there was formed the mixture of two epimeric monoacetates of triols (XXX) and (XXXI). The normal oxidation products – acetates of glycidic alcohol (XXXII) – were not isolated in this reaction.



(XXVIII) (XXX) (XXXI) (XXXII)

It was shown by alkaline hydrolysis of acetates (XXX) and (XXXI) that they contain one acetyl group. In this reaction, from the hydrolysis products of acetate (XXX) there was isolated the above-described triol (XII). Acetate (XXXI) gave the above-described triol (XIV) on hydrolysis.

A similar result was obtained in oxidation of the trans-acetate (XXIX).

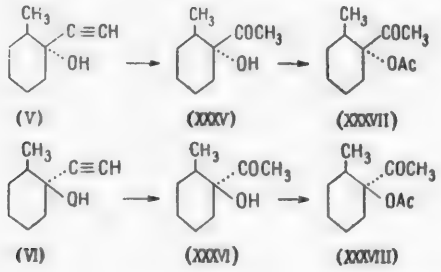


(XXIX) (XXXIV) (XXXIII)

In this case, instead of the expected acetate of the glycidic alcohol (XXXIII), there was isolated a liquid mixture of acetates of isomeric triols (XXXIV), on the hydrolysis of which there were obtained the above-described triol (XXIII) and an unknown triol (XXXVII), with m.p. 112°. Triol (XVII) was obtained in the greater amount. These results testify that the oxidation of acetates of tertiary vinyl alcohols with peracetic acid, in contrast to the oxidation of the corresponding vinyl alcohols and acetates of allylic alcohols, proceeds differently and does not lead to the formation of normal oxidation products – acetates of glycidic alcohols [1]. Theory predicts for the epimeric pair of vinyl alcohols (XXIII) and (XXV) the possibility of formation of four racemic triols (three asymmetric centers exist in the molecule). We isolated three crystalline triols (XX), (XXII), and (XXVII) in the trans-series. This result testifies that there takes place here, evidently, a phenomenon of polymorphism or the formation of mixed crystals of (XXVII) with m.p. 112°.

Conformational analysis permits one to connect, as it is known, the stereochemistry of a molecule with its reactivity [9]. Therefore it was of interest to study the reaction of hydration of the triple bond on the examples of the pair of epimeric acetylenic alcohols (V) and (VI), as well as to study the acetylation of the tertiary hydroxyl with the purpose of establishment of the dependence of the reaction rate on the equatorial or the axial disposition of the substituent. On hydration of cis-alcohol (V) in methanolic solution in the presence of mercuric sulfate and sulfuric acid, there was formed in almost quantitative yield the cis-α-ketol (XXXV) with m.p. 37-38°, which had been prepared earlier [4].

Trans-alcohol (VI) hydrates into liquid trans-α-ketol (XXXVI) at a somewhat greater rate but in lower yield.



(V) (XXXV) (XXXVII)

(VI) (XXXVI) (XXXVIII)

A greater distinction is observed in the reaction of acetylation of the hydroxyl group in the epimeric pair of α-ketols (XXXV) and (XXXVI). In case of cis-α-ketol (XXXV) the acetylation proceeds under mild conditions by refluxing with excess acetyl chloride in ether. Under these conditions the trans-α-ketol (XXXVI) does not acetylate at all. We failed to esterify it under even more drastic conditions – with acetyl chloride in pyridine. Only by the action of acetic anhydride in the presence of concentrated sulfuric acid could acetylation of the hydroxyl in trans-α-ketol (XXXVI) be made to take place. The yields of acetates (XXXVII) and (XXXVIII) were close to the theoretical.

This result testifies that in the cis-α-ketol (XXXV) the tertiary hydroxyl is evidently in the equatorial configuration, while in the trans-α-ketol (XXXVI) it has the axial position [9, 10].

EXPERIMENTAL

Acetate of cis-2-methyl-1-ethynyl-1-cyclohexanol (VII). A solution of 200 g of cis-alcohol (V) (m.p. 56-57°) and 800 g of freshly distilled acetic anhydride was refluxed for three hours. After cooling, the excess acetic anhydride was distilled off in vacuum, the residue was dissolved in ether, neutralized with a sodium bicarbonate solution and dried with sodium sulfate. There was obtained 207 g of the acetate of cis-2-methyl-1-ethynyl-1-cyclohexanol (VII) in the form of a colorless liquid with b.p. 102-103° (15 mm), $n^{18}D$ 1.4675.

Acetate of trans-2-methyl-1-ethynyl-1-cyclohexanol (XV). From 250 g of alcohol (VI) and 1000 g of acetic anhydride there was obtained, under the above-described conditions, 255 g, of the acetate of trans-2-methyl-1-ethynyl-1-cyclohexanol (XV) in the form of a colorless liquid with b.p. 98-102° (18 mm), $n^{18}D$ 1.4650.

Acetate of cis-2-methyl-1(ω-dibromoacetyl)-1-cyclohexanol (VIII). To the aqueous solution of bromoacetamide [1], obtained from 60 g of acetamide and 150 g of bromine in 300 ml of water, there was added 50 g of sodium acetate and 30 ml of glacial acetic acid, after which there was added 35 g of acetate (VII). The temperature of the reaction mixture was kept from rising above 25° by suitable cooling. After two hours, the precipitated reaction product was separated and dissolved in ether. The ethereal solution was neutralized with sodium bicarbonate and dried with sodium sulfate. There was obtained 70 g of crystals from which there was isolated, after crystallization from petroleum ether, 62 g of cis-dibromoketol (VIII) in the form of colorless crystals with m.p. 90-90.5°.

Found %: C 37.24, 37.06; H 4.34, 4.40; Br 45.06, 45.37. $C_{11}H_{18}O_3Br_2$. Calculated %: C 37.10; H 4.49; Br 44.64.

Rearrangement of the acetate of cis-dibromoketol (VIII). Preparation of cis-dihydroxycarboxylic acids: cis-2-methyl-1-hydroxycyclohexylglycolic acids (erythro-threo isomerism) (IX) and (X). To the solution of 120 g of barium hydroxide in 200 ml of water there was added dropwise at 70-75° and with energetic stirring a solution of 58 g of cis-dibromoketol (VIII) in 150 ml of trimethylcarbinol. A rise in the temperature of the reaction mixture was observed (to 80-85°), this temperature being maintained for 5-7 minutes despite cooling the reaction flask with cold water. After cooling, the solution was filtered, the filtrate was evaporated to dryness in vacuum and the residue was extracted with ether to remove the neutral products. Then the residue was treated with 15% hydrochloric acid and the precipitated acids were extracted with ether. There was obtained 7 g of liquid products and 12.5 g of crystals, which after fractional recrystallization from ether, petroleum ether and iso-octane, gave two isomeric cis-dihydroxycarboxylic acids (IX) and (X). The dihydroxy acid (IX), which formed colorless crystals with m.p. 149.5-150° (from ether) was isolated in the predominant amount.

Found %: C 57.42, 57.64; H 8.51, 8.62. $C_9H_{16}O_4$. Calculated %: C 57.45; H 8.51.

The dihydroxy acid (X), which was isolated in a small amount, melted at 128.5-129° (from ether).

Found %: C 57.64, 57.53; H 8.44, 8.42. $C_9H_{16}O_4$. Calculated %: C 57.45; H 8.51.

The mixed melting point of acids (IX) and (X) was 102-120°. These acids form a difficultly separable mixture with a stable m.p. 117-118° (from chloroform).

Acetate of trans-2-methyl-1(ω-dibromoacetyl)-1-cyclohexanol (XVI). By the action of an aqueous solution of bromoacetamide, prepared as shown above from 85 g of acetamide and 220 g of bromine in 300 ml of water, on 60 g of acetate (XV) (b.p. 98-102° at 18 mm) there was obtained 116 g of trans-dibromoketol (XVI) in the form of nearly colorless viscous oil with b.p. 152-153° (3 mm), $n^{20}D$ 1.5275.

Found %: C 36.93, 36.82; H 4.27, 4.38; Br 44.83, 44.69. $C_{11}H_{16}O_2Br_2$. Calculated %: C 37.10; H 4.49; Br 44.64.

Rearrangement of the acetate of trans-dibromoketol (XVI). Preparation of trans-dihydroxy carboxylic acids: trans-2-methyl-1-hydroxycyclohexyl-glycolic acids (erythro-threo isomerism) (XVII) and (XVIII). By hydrolysis of 70 g of the acetate of trans-dibromoketol (XVI) with barium hydroxide under conditions described above there was isolated 18 g (the yield was about 50% of the isomeric mixture) of two isomeric trans-dihydroxy carboxylic acids – (XVII) and (XVIII). The dihydroxy acid (XVII), which was isolated in the predominant amount, melted at 156-156.5° (from ether).

Found %: C 57.46, 57.28; H 8.63, 8.65. $C_9H_{16}O_4$. Calculated %: C 57.45; H 8.51.

Dihydroxy acid (XVIII) melted at 109.5-110° (from chloroform).

Found %: C 57.60, 57.58; H 8.56, 8.36. $C_9H_{16}O_4$. Calculated %: C 57.45; H 8.51.

Acids (XVII) and (XVIII) form a difficultly separable mixture with a stable m.p. 103-104° (from chloroform). Mixed melting point of these acids melted at 102-133°.

Methyl ester of the cis-dihydroxy acid (XI). To a solution of 2 g of cis-dihydroxy acid (IX) (m.p. 149.5-150°) in 100 ml of ether there was added the ethereal solution of diazomethane prepared from 16 g of nitrosomethylurea. On the following day, after distillation of ether, there was obtained about 2 g of the methyl ester of (XI) in the form of a viscous colorless oil which was subjected to reduction without further purification.

Reduction of methyl ester (XI) with lithium aluminum hydride to the triol – cis-2-methyl-1-hydroxycyclohexyl glycol (m.p. 88°) (XII). Into a three-necked flask provided with a mechanical stirrer, a reflux condenser, a calcium chloride tube and a dropping funnel, there was placed 1 g of lithium aluminum hydride in 200 ml of absolute ether (a suspension) and to this there was added from the dropping funnel with continued stirring over ten minutes an ethereal solution of 1 g of methyl ester (XI). Then the reaction mixture was refluxed for three hours and allowed to stand overnight at room temperature. On the following day 5 ml of ethyl acetate was added with cooling and the product was treated with 20 ml of 10% sulfuric acid, extracted with ether, washed with a solution of sodium bicarbonate and dried with sodium sulfate. After distillation of ether there was obtained 0.9 g of a sirup, which crystallized after addition of ether. Recrystallization from a mixture of ether with petroleum ether gave 0.6 g of triol (XII) with m.p. 88-88.5°. Some 0.3 g of crystals of the triol was obtained in addition from the mother liquor.

Found %: C 62.06, 62.07; H 10.23, 10.33. $C_9H_{18}O_3$. Calculated %: C 62.07; H 10.35.

Methyl ester (XIII). By the action of an ethereal solution of diazomethane there was obtained from 0.09 g of acid (X) (m.p. 128.5-129°) 0.05 g of methyl ester (XIII) in the form of prisms with m.p. 73-74° (from petroleum ether).

Reduction of methyl ester (XIII) with lithium aluminum hydride into triol – cis-2-methyl-1-hydroxycyclohexyl glycol (m.p. 90°) (XIV). By the reduction of 0.05 g of methyl ester (XIII) with m.p. 73-74° with lithium aluminum hydride, as described above (refluxing for seven hours) there was obtained 0.02 g of crystals with m.p. 82-87° (from iso-octane). After repeated crystallization from iso-octane there was isolated the triol (XIV) with m.p. 90-90.5°.

Found %: C 61.72, 61.85; H 10.33, 10.36. $C_9H_{18}O_3$. Calculated %: C 62.07; H 10.35.

The mixed melting point with isomeric triol (XII) was 50-55°.

Methyl ester of trans-acid (XIX). From 2 g of trans-acid (XVII) (m.p. 156-156.5°) there was obtained by the action of an ethereal solution of diazomethane 1.9 g of methyl ester (XIX) in the form of colorless needles with m.p. 91-91.5° (ether + petroleum ether).

Found %: C 59.37, 59.23; H 8.92, 8.86. $C_{10}H_{18}O_4$. Calculated %: C 59.41; H 8.91.

Reduction of methyl ester (XIX) to the triol: trans-2-methyl-1-hydroxycyclohexyl glycol (m.p. 125°). Methyl ester (XIX) (0.85 g) was reduced with a four-fold excess of lithium aluminum hydride as described above. There was obtained 0.6 g of the triol (XX) in the form of colorless prisms with m.p. 125-125.5°.

Found %: C 61.67, 61.75; H 10.30, 10.36. $C_9H_{18}O_3$. Calculated %: C 62.07; H 10.35.

From the mother liquor there was isolated an additional 0.1 g of the triol (XX) with m.p. 120-123°.

Methyl ester of trans-acid (XXI). By the action of diazomethane, as described above, there was prepared from 0.4 g of trans-acid (XVIII) (m.p. 109.5-110°) 0.4 g of methyl ester (XXI) with m.p. 53-54° (from iso-octane). The entire amount of the methyl ester was used for the reduction.

Reduction of methyl ester (XXI) into triol: (trans-2-methyl-1-hydroxycyclohexyl glycol (m.p. 88.5°) (XXII). By reduction of 0.4 g of methyl ester (XXI) (m.p. 53-54°) by a four-fold excess of lithium aluminum hydride, as described above (refluxed for nine hours) there was obtained about 0.2 g of crystals with m.p. 76-78° and 0.05 g of crystals with m.p. 86-87° (rhombic plates). A mixed melting point of the two was 77-79°. After recrystallization from a mixture of ether and petroleum ether of the crystals with m.p. 76-78° there was obtained 0.1 g of triol (XXII) with the same melting point. An additional recrystallization from high-boiling petroleum ether, with preliminary melting of the sample, gave crystals with m.p. 88-88.5° (needles).

Found %: C 62.24, 62.13; H 10.46, 10.24. $C_9H_{18}O_3$. Calculated %: C 62.07; H 10.35.

Triol (XXII) gave a large depression in mixed melting points with the triols prepared above (XII) and (XIV) with m.p. respectively, 88-88.5° and 90-90.5° (the mixed melting points were 55-65° and 50-62°).

Preparation of cis-1-vinyl-2-methyl-1-cyclohexanol (XXIII). Cis-acetylenic alcohol (V) (220 g) (m.p. 56-57°) was hydrogenated in 100 ml of methanol over 2.5 hours under hydrogen pressure of 4 atm in a reactor with a stirrer in the presence of 0.25 g of $Pd/CaCO_3$ (about 5% palladium) until the calculated amount of hydrogen was absorbed (38 l). The end of hydrogenation was controlled by an acetylenic test. There was obtained 219 g of the vinyl alcohol (XXIII) [8] in the form of a colorless liquid with b.p. 87-87.5° (21 mm), $n^{21}D$ 1.4767.

Cis-1-ethyl-2-methyl-1-cyclohexanol was obtained in the form of a colorless liquid with b.p. 76-76.5° 11.5 mm), $n^{18}D$ 1.4712 [11] after exhaustive hydrogenation of acetylenic alcohol (V).

Synthesis of trans-1-vinyl-2-methyl-1-cyclohexanol (XXV). On hydrogenation of 304 g of liquid acetylenic trans-alcohol (VI) (b.p. 75° at 15 mm, $n^{18}D$ 1.4770) in the presence of 0.33 g of palladium catalysts, analogously to above, (the hydrogenation was interrupted after absorption of 53 liters of hydrogen) there was obtained after a vacuum distillation 280 g of trans-vinyl alcohol (XXV) in the form of a colorless liquid with b.p. 65-67° (8 mm), $n^{22}D$ 1.4720.

On exhaustive hydrogenation of acetylenic alcohol (VI) there was obtained trans-1-ethyl-2-methyl-1-cyclohexanol in the form of a colorless liquid with b.p. 71-72° (11 mm), $n^{19}D$ 1.4683.

Oxidation of cis-vinyl alcohol (XXIII) with peracetic acid. To the solution of 20 g of vinyl alcohol (XXIII) (b.p. 87-87.5° at 21 mm, $n^{21}D$ 1.4767) in 100 ml of chloroform there was added 13.5 g of 90% peracetic acid (10% excess). The reaction temperature was maintained at 20° with water cooling. After four hours there formed an upper layer of a colorless liquid. The oxidation reaction was completed after three days. At this time there remained in the reaction mixture some 2.4 g of peracetic acid (the added excess was 1.8 g). The solution was neutralized with aqueous sodium bicarbonate and dried with sodium sulfate. After vacuum distillation there was obtained 19.5 g of a colorless liquid with b.p. 88-91° (6 mm), $n^{14}D$ 1.4757, which consisted of a mixture of glycidic alcohols. After prolonged freezing of the mixture we succeeded in isolating some 10 g of the glycidol (XXIV) with m.p. 43-43.5° (from petroleum ether).

Found %: C 69.00, 69.12; H 10.16, 10.10. $C_9H_{16}O_2$. Calculated %: C 69.87; H 10.26.

As the result of fractional vacuum distillation there was obtained from the liquid portion, amounting to 8 g, some liquid glycidol (XXIV).

B.p. 89-90° (7 mm), $n^{20}D$ 1.4780, d^{20}_4 1.0389. MR_D 42.50. Calculated 42.53 (without the oxide ring increment).

Found %: C 68.90, 69.03; H 10.26, 10.42. $C_9H_{16}O_2$. Calculated %: C 69.23; H 10.26.

In iodometric determination of the unreacted peracetic acid in this experiment there was isolated a substance with m.p. 115-116° (decomposition) (from ether + petroleum ether), which was the product of addition of hydroiodic acid to the glycidic alcohol.

Found %: C 37.95, 38.09; H 6.09, 6.08; I 44.67, 44.75. $C_9H_{17}O_2I$. Calculated %: C 38.04; H 5.98; I 44.70.

Oxidation of trans-vinyl alcohol (XXV) with peracetic acid. On oxidation of 20 g of trans-vinyl alcohol (XXV) with peracetic acid, as described above, there was obtained 20 g of a colorless, viscous, partly crystallizable liquid, from which, after repeated freezing, there was isolated 10 g of crystalline glycidol (XXVI) with m.p. 75-75.5° (from petroleum ether).

Found %: C 69.25, 69.50; H 10.49, 10.46. $C_9H_{16}O_2$. Calculated %: C 69.23; H 10.26.

Mixed melting point with glycidol (XXIV) (m.p. 43°) was 35-37°.

After separation of the crystals with m.p. 75° from the liquid reaction product and a vacuum distillation through a column there was obtained 2 g of low-melting glycidol (XXVI) in the form of a colorless viscous oil.

B.p. 86-87° (7 mm), $n^{20}D$ 1.4715, d^{20}_4 1.0253. MR_D 42.57; calculated 42.53 (without the oxide ring increment). M.p. 40.5-41° (petroleum ether).

Found %: C 69.37, 69.51; H 10.30, 10.41. $C_9H_{16}O_2$. Calculated %: C 69.23; H 10.26.

After prolonged standing of the liquid glycidol there was observed some crystallization with formation of crystals of glycidol (XXVI) with m.p. 40.5-41°. Mixed melting point with the high-melting glycidol (m.p. 75°) was 35-36°. Mixed melting point with (XXIV) (m.p. 43.5°) was 20°.

Hydrolysis of crystalline cis-2-methyl-1-hydroxycyclohexylethylene oxide (m.p. 43°) (XXIV) into triol (XII). Cis-glycidol (XXIV) with m.p. 42.5-43° (0.53 g) in 100 ml of distilled water containing 2 ml of glacial acetic acid was refluxed for three hours. After filtration the solution was evaporated in vacuum, leaving as a residue 0.6 g of a viscous sirup on recrystallization of which from a mixture of ether and petroleum ether there was isolated 0.3 g of triol (XII) with m.p. 88-88.5°, which did not give a depression in mixed melting point with the specimen prepared above. In addition to the crystals there was obtained in this experiment some 0.25 g of an uncrystallizable sirup. The liquid glycidol (XXIV) under these conditions gave a viscous, difficultly recrystallizing sirup, from which there was isolated, in a small amount, the triol (XIV) with m.p. 90-90.5°, which did not give a depression in mixed melting point with the above described specimen.

Hydrolysis of high-melting trans-2-methyl-1-hydroxycyclohexylethylene oxide (m.p. 75°) (XXVI) into triol (XX). One g of the trans-glycidol (XXVI) (m.p. 75°) was hydrolyzed with 40 ml distilled water containing 3 ml

of glacial acetic acid, as described above. There was obtained thereby 0.7 g of triol (XX) with m.p. 124-125° (from ether) which did not give a depression in mixed melting point with the specimen described above. There was isolated about 0.2 g of triol (XX), additionally, from the mother liquor; this had m.p. 122-123°.

Hydrolysis of trans-glycidol (XXVI) (m.p. 41°) into triol (XXII). Refluxing 0.3 g of glycidol (XXVI) (m.p. 40-41°) for ten hours with 30 ml of water containing 2 ml of glacial acetic acid, followed by cooling the solution, neutralization with sodium bicarbonate and evaporation in vacuum to dryness, and finally extraction of the residue with ether gave 0.25 g of triol (XXII) in the form of colorless prisms with m.p. 111.5-112° (from ether). On hydrolysis of the liquid mixture of glycidols (XXVI) there was isolated triol (XXVII) with m.p. 111.5-112° (from ether).

Found %: C 62.10, 62.18; H 10.37, 10.38. $C_9H_{18}O_3$. Calculated %: C 62.07; H 10.35.

Mixed melting point with triol (XX), whose m.p. is 125-125.5°, was found to be 109-120°.

Acetate of cis-2-methyl-1-vinyl-1-cyclohexanol (XXVIII). Forty four g of the acetate of cis-acetylenic alcohol (VII) was selectively hydrogenated in an equal volume of methanol over palladium catalysts (0.25 g of 5% $Pd/CaCO_3$). The calculated amount of hydrogen was absorbed in four hours (5.75 liters) and the hydrogenation was terminated. Acetate (VII) hydrogenates noticeably more rapidly than does the acetylenic alcohol (V). There was obtained 41 g of the acetate of cis-2-methyl-1-vinyl-1-cyclohexanol (XXVIII) in the form of a colorless liquid.

B.p. 78-78.5° (6 mm), $n^{20}D$ 1.4611.
Found %: C 72.63, 72.54; H 9.92, 9.90. $C_{11}H_{18}O_2$. Calculated %: C 72.53; H 9.89.

Acetate of trans-2-methyl-1-vinyl-1-cyclohexanol (XXIX). Transacetate (XV) (41.6 g) was selectively hydrogenated in 46 ml of methanol over palladium catalyst as described above. The hydrogenation of the trans-acetate (XV) proceeds more rapidly than does that of the cis-acetate (VII) and was completed in three hours. There was obtained 34 g of the acetate of trans-2-methyl-1-vinyl-1-cyclohexanol (XXIX) in the form of a colorless liquid.

B.p. 75-78° (7 mm), $n^{20}D$ 1.4597.
Found %: C 72.47, 72.36; H 9.74, 9.60. $C_{11}H_{18}O_2$. Calculated %: C 72.53; H 9.89.

Oxidation of cis-2-methyl-1-vinyl-1-cyclohexyl- acetate (XXVIII) with peracetic acid. To the solution of 12.7 g of acetate (XXVIII) (b.p. 79° at 6 mm, $n^{20}D$ 1.4611) in 50 ml of chloroform there was added, at 0°, 10 g of 90% peracetic acid and the mixture was left for one month at room temperature. No elevation of temperature of the mixture was observed. After one month the solution contained about 2 g of peracetic acid (the added excess was 2 g). The solution was neutralized with aqueous sodium bicarbonate and dried with sodium sulfate. After a vacuum distillation there was obtained about 3 g of the initial acetate (XXVIII) with b.p. 82-85° (7 mm) and 6.7 g of a viscous colorless sirup with b.p. 145-146° (3 mm), $n^{17}D$ 1.4862, which crystallized gradually. After several recrystallizations from a mixture of ether with petroleum ether there was isolated 1.7 g of colorless crystals consisting of a mixture of crystals of two different forms: prisms with m.p. 58.5-59.5° (0.9 g) and long needles with m.p. 71-72° (0.75 g). By further recrystallization from petroleum ether the fraction with m.p. 71-72° yielded the acetate of the triol (XXX) in the form of silvery white needles with m.p. 99-100°.

Found %: C 61.04, 61.05; H 9.22, 9.24. $C_{11}H_{20}O_4$. Calculated %: C 61.11; H 9.26.

The acetate of triol (XXXI) was isolated in the form of silvery white needles with m.p. 57-58°, after several recrystallizations of the fraction with m.p. 58.5-59.5° from petroleum ether.

Found %: C 61.22, 61.37; H 9.32, 9.33. $C_{11}H_{20}O_4$. Calculated %: C 61.11; H 9.26.

The mixed melting point with acetate (XXX) (m.p. 99-100°) was 57.5-85°. Acetate (XXXI) is more difficultly soluble in petroleum ether than is acetate (XXX).

Hydrolysis of cis-2-methyl-1-acetoxycyclohexyl glycol (XXX) (m.p. 99-100°) into triol (XII). The solution of 0.15 g of acetate (XXX) (m.p. 99-100°) in 20 ml of ethanol was refluxed for four hours with 10 ml of 0.5 N alcoholic solution of potassium hydroxide. The excess alkali was back titrated on the following day with 0.1 N solution of sulfuric acid. Six and eight tenths ml of 0.1 N solution of potassium hydroxide was consumed in the hydrolysis, which amount corresponded to one acetate group. After neutralization of the solution, followed by

evaporation and extraction, with a subsequent crystallization from petroleum ether, there was isolated 0.08 g of triol (XII) with m.p.87-88°, which did not give a mixed melting point depression with a specimen described above. The hydrolysis of acetate (XXX) does not proceed to completion after boiling for one hour.

Hydrolysis of cis-2-methyl-1-acetoxycyclohexyl glycol (m.p. 57-58°) (XXXI) into triol (XIV). Acetate (XXXI) (m.p. 57-58°) (0.36 g) and 10 ml of 0.5 N alcoholic solution of potassium hydroxide were refluxed for one hour. Henceforth the experiment was conducted as described above. The consumption of 0.1 N solution of potassium hydroxide for the hydrolysis was 16.7 ml, which amount corresponded to the presence in it of one acetate group. From the solution there was isolated, by evaporation and extraction with ether, 0.04 g of triol (XIV) with m.p. 90-90.5°, which did not give a depression of mixed melting point with a specimen described above. An additional amount of 0.2 g of crystals with m.p. 71-72° was isolated from the mother liquor.

Oxidation of the acetate of trans-2-methyl-1-vinyl-1-cyclohexanol (XXIX) with peracetic acid. By an oxidation of 12.7 g of acetate (XXIX) (b.p. 75-80° at 7 mm, $n^{20}D$ 1.4595) in 50 ml of chloroform with 10 g of 90% peracetic acid, as described above, there was obtained about 5 g of a mixture of acetates of triol (XXXIV) in the form of a colorless uncrystallizable sirup.

B.p. 148.5-149° (4 mm), $n^{20}D$ 1.4850.

Found %: C 61.27, 61.43; H 9.30, 9.22. $C_{11}H_{20}O_4$. Calculated %: C 61.11; H 9.26.

Hydrolysis of the mixture of trans-2-methyl-1-acetoxycyclohexyl glycols (XXXIV). Preparation of triols (XXII) and (XXVII). A solution of 1.81 g of the above described mixture of acetates (XXXIV) (b.p. 148.5-149° at 4 mm) in 50 ml of 0.5 N alcoholic solution of potassium hydroxide was refluxed for two hours. Eighty four ml of 0.1 N potassium hydroxide solution was consumed in the hydrolysis, which amount corresponded to the presence of one acetate group in acetate (XXXIV). The neutralized solution was worked up as indicated above. Hereby there was obtained 0.7 g of crystals with m.p. 105-108° and 0.7 g of partly crystallizable sirup. By additional crystallizations from a mixture of ether and iso-octane, fraction with m.p. 105-108° gave 0.35 g of triol (XXVII) in the form of colorless plates with m.p. 111.5-112°, which did not give a depression of mixed melting point with the above described specimen. From the mother liquor there was isolated 0.05 g of triol (XXII) in the form of silvery white crystals with m.p.86-87° (from petroleum ether, b.p. 95-110°).

Found %: C 62.24, 62.13; H 10.46, 10.24. $C_9H_{18}O_3$. Calculated %: C 62.07; H 10.35.

A mixed melting point with the sample of triol (XXII), obtained above, (m.p. 88-88.5°) was 87-88°. Mixed melting point with triol (XXVII) (m.p. 111.5-112°) was 86-109° (moistens at 85°). Mixed melting point with triol (XII) (m.p. 88-88.5°) was 55-60°. Mixed melting point with triol (XIV) (m.p. 90-90.5°) was 20° (took place during rubbing of the specimen on glass). Mixed melting point with triol (XX) (m.p. 125-125.5°) was 108-114°.

Hydration of cis-2-methyl-1-ethynyl-1-cyclohexanol (V). A solution of 28 g of cis-acetylenic alcohol (V) (m.p. 56-57°) in 100 ml of methanol was added with stirring over one hour at 18° to an aqueous methanolic solution of 10 g of mercuric sulfate and 25 g of concentrated sulfuric acid (in 100 g of water and 75 ml of methanol). The formation of a white cheesy precipitate was observed. The reaction temperature was maintained at 18-19°. The hydration reaction was controlled by the acetylenic test (formation of silver acetylide with ammoniacal solution of silver nitrate). The acetylenic test was positive after five hours. The reaction mixture was stirred for 6.5 hours at 19°, on the following day, until the acetylenic test became negative. The solution was diluted to twice the volume with water, neutralized with sodium bicarbonate, filtered and evaporated in vacuum. The residue was extracted with ether, dried with sodium sulfate and distilled. There was obtained 25 g of cis-2-methyl-1-acetyl-1-cyclohexanol (XXXV) in the form of colorless viscous liquid.

B.p. 92-93° (8 mm),* m.p. 37-38° (from petroleum ether), $n^{20}D$ 1.4735, d^{20}_4 1.0226, MR_D 42.83; calculated 43.10.

Semicarbazone of (XXXV) formed small colorless crystals with m.p. 228-229° (from ethanol) [4].

Acetate of cis-2-methyl-1-acetyl-1-cyclohexanol (XXXVII). To the solution of 10 g of α-ketol (XXXV) (m.p. 37-38°) in 50 ml of ether there was added 20 g of acetyl chloride and the solution was refluxed for four hours with protection from access of moisture by means of a calcium chloride tube. The yellowish solution was

*Author of [4] mistakenly assigned the lower b.p. (81-82° at 12 mm) to the crystalline isomer.

then evaporated in vacuum and the residue was distilled in vacuum. There was obtained 11 g of the acetate of cis-2-methyl-1-acetyl-1-cyclohexanol (XXXVII) in the form of a colorless liquid.

B.p. 121-122° (12 mm), $n^{20}D$ 1.4629, d^{20}_4 1.0470. MR_D 52.58; calculated 52.46.
Found %: C 66.90, 66.72; H 9.27, 9.15. $C_{11}H_{18}O_3$. Calculated %: C 66.66; H 9.10.

The same result was obtained in acetylation of α-ketol (XXXV) with acetic anhydride in the presence of one drop of sulfuric acid. The acetate (XXXVII) does not form a 2,4-dinitrophenylhydrazone.

Hydration of trans-2-methyl-1-ethynyl-1-cyclohexanol (VI). Trans-acetylenic alcohol (VI) (b.p. 70° at 10 mm, $n^{17}D$ 1.4777) (28 g) was hydrated at room temperature in the presence of mercuric sulfate and concentrated sulfuric acid as described above. The hydration was completed in 5.5 hours (negative test for acetylenic hydrogen with ammoniacal solution of silver nitrate). There was obtained 16 g of trans-2-methyl-1-acetyl-1-cyclohexanol (XXXVI) in the form of a colorless liquid.

B.p. 82-83° (10 mm), $n^{20}D$ 1.4620, d^{20}_4 0.9974. MR_D 43.0; calculated 43.10 [4].
Literature data [4]: b.p. 92° (10 mm),* $n^{20}D$ 1.4635.
Found %: C 68.91, 68.71; H 10.40, 10.36. $C_9H_{16}O_2$. Calculated %: C 69.23; H 10.34.

A somewhat better yield of trans-α-ketol (XXXVI) was obtained in the hydration of acetylenic alcohol (VI) at the temperature of 60-72°.

Semicarbazone of trans-α-ketol (XXXVI) forms colorless crystals with m.p. 217-218° (from ethanol) [4]. Mixed melting point with semicarbazone of cis-α-ketol (XXXV) (m.p. 228-229°) was 200-203°.

The liquid trans-α-ketol (XXXVI) has a lower boiling point, index of refraction and specific gravity than does the crystalline cis-isomer (XXXV). This fact indicates that the Auwers-Skita rule is applicable to 1,2-gem substituted cyclohexanes as well.

Acetate of trans-2-methyl-1-acetyl-1-cyclohexanol (XXXVIII). To 20 g of freshly distilled acetic anhydride containing one drop of concentrated sulfuric acid there was added dropwise 10 g of trans-α-ketol (XXXVI) (b.p. 80-86° at 10 mm, $n^{18}D$ 1.4630). The reaction temperature was kept from rising above 20° by means of water cooling. On the following day the solution was heated for two hours to 50-70°, diluted with four volumes of water, neutralized with sodium bicarbonate, extracted with ether and dried over sodium sulfate. There was obtained 10 g of the acetate of trans-2-methyl-1-acetyl-1-cyclohexanol (XXXVIII) in the form of a colorless liquid.

B.p. 115.5-116.5° (12 mm), $n^{20}D$ 1.4590, d^{20}_4 1.0383. MR_D 52.13; calculated 52.46.
Found %: C 66.22, 66.20; H 8.99, 9.10. $C_{11}H_{18}O_3$. Calculated %: C 66.66; H 9.10.

Acetate (XXXVIII) does not form a 2,4-dinitrophenylhydrazone.

Trans-α-ketol (XXXVI) is not acetylated by acetyl chloride in ether and in pyridine, as well as by refluxing with acetic anhydride without a catalyst.

SUMMARY

1. The stereochemistry of reactions of introduction of dihydroxycarboxylic, glyceryl and α-ketolic side chains was studiedwith the example of o-methylcyclohexanone.

2. It was shown for the first time that the intramolecular rearrangement of acetates of cis- and trans-2-methyl-1(ω-dibromoacetyl)-1-cyclohexanol does not proceed stereospecifically but forms all four racemic dihydroxy carboxylic acids which are predictable by theory – cis-2-methyl-1-hydroxycyclohexylglycolic acids (erythro-threo isomerism) and trans-2-methyl-1-hydroxycyclohexylglycolic acids (erythro-threo isomerism).

3. The reduction of the indicated dihydroxy acids with lithium aluminum hydride was accomplished, yielding the corresponding triols: cis-2-methyl-1-hydroxycyclohexyl glycols (erythro-threo isomerism) and

*Evidently the higher boiling point, which pertains to the cis-isomer, was mistakenly assigned to the trans-isomer.

trans-2-methyl-1-hydroxycyclohexyl glycols (erythro-threo isomerism), which were obtained also by the hydrolysis of stereoisomeric glycidic alcohols – cis- and trans-2-methyl-1-hydroxycyclohexylethylene oxide (erythro-threo isomerism).

4. It was shown that in contrast to tertiary vinyl alcohols, the cis- and trans-vinyl-2-methyl-cyclohexanols, the oxidation of the acetates of these alcohols with peracetic acid proceeds anomalously and, instead of the expected glycidols, yields two cis-2-methyl-1-acetoxycyclohexyl glycols and two trans-2-methyl-1-acetoxycyclohexyl glycols.

5. On the basis of the difference in the rate of acetylation of the cis- and the trans-α-ketols a supposition is expressed about the equatorial and axial conformations of the hydroxyl in cis-2-methyl-1-acetyl-1-cyclohexanol and trans-2-methyl-1-acetyl-1-cyclohexanol respectively.

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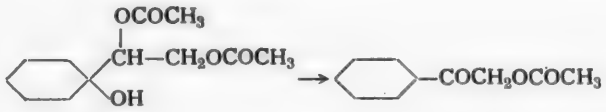
A STUDY IN THE FIELD OF STEREOCHEMISTRY OF CYCLIC COMPOUNDS

28. STERIC DIRECTIVITY OF THE SERINI REACTION IN THE CYCLOHEXANE SERIES

I. N. Nazarov, A. A. Akhrem and A. V. Kamernitskii

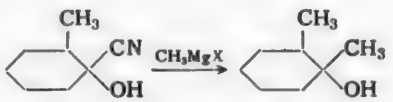
The rearrangement of the secondary monoacetate of secondary-tertiary α-glycols, under the influence of zinc dust, into ketones with the same carbon skeleton, which is known under the name of the Serini reaction, has been studied extensively in the steroid series [1], in which it proceeds strictly stereospecifically and leads to the inversion of configuration at the tertiary carbon atom. The Serini reaction is at present a dependable method of determination of the configuration of the side chain at the 17-carbon atom of steroids.

However to this date there have been no studies devoted to the stereochemistry of the Serini reaction in the series of the simplest cyclic compounds. The only known instance of the transformation of 2,3-diacetate of 1-pentamethyleneglycerol into acetoxymethyl cyclohexyl ketone [2] does not permit one to draw any stereochemical deductions.

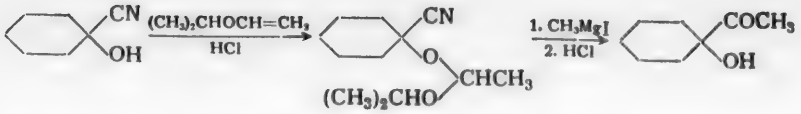


Insofar as it has been established by us [3, 4] the steric structure of isomeric 1-acetyl-2-methylcyclohexanols, which contain two asymmetric centers, appeared to be an example with which one may realize the Serini reaction with interesting results.

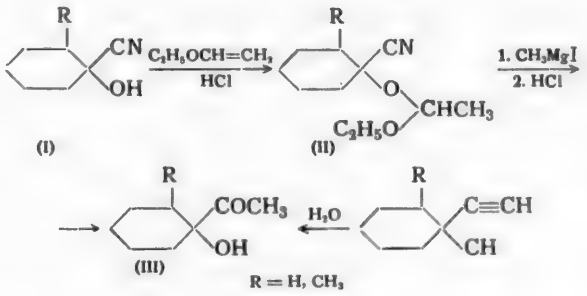
1-Acetyl-2-methylcyclohexanols were prepared both by hydration of 1-ethynyl-2-methylcyclohexanols [4], and by the reaction of cyanohydrins of 2-methylcyclohexanone with methylmagnesium iodide. This permitted us to relate among themselves the stereoisomeric cyanohydrins and acetylenic alcohols derived from 2-methylcyclohexanone, by additional routes. It is known that the direct reaction of cyanohydrins of 2-methylcyclohexanone with methylmagnesium halides leads to decomposition of the cyanohydrins and to formation of the corresponding alcohol [5].



It was shown recently, with the example of cyclohexanone cyanohydrin [6], that a preliminary protection of the hydroxyl group with dihydropyran permits one to conduct a normal reaction with organomagnesium compounds. There is also the communication [7] in which there is indicated the possibility of application, for the hydroxyl protection, of vinyl isopropyl ether.

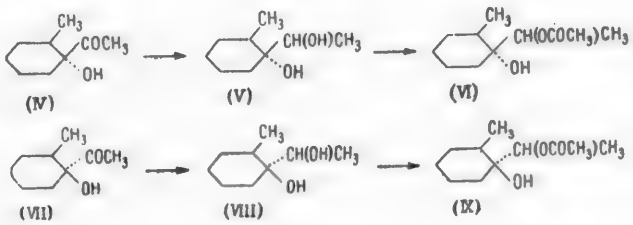


We realize the reaction of cyanohydrins of cyclohexanone and cis- and trans-cyanohydrins of 2-methylcyclohexanone with methylmagnesium iodide with the preliminary protection of the hydroxyl group of the cyanohydrins by means of vinyl ethyl ether. The reaction of cyanohydrins (I) with vinyl ethyl ether was run in anhydrous benzene in the presence of an ethereal solution of hydrogen chloride; thereby there were prepared the corresponding acetals (II).



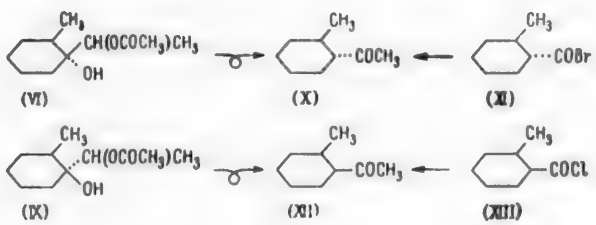
By the action of methylmagnesium iodide on acetals (II) there were prepared in 75% yield of acetylcyclohexanols (III) which were identical with the ketols formed by hydration of the corresponding acetylenic alcohols.

Stereoisomeric 1-acetyl-2-methylcyclohexanols (IV) and (VII) were subjected to reduction with aluminum isopropoxide in toluene solution with distillation of acetone. Hereby from cis-ketol (IV) there was obtained only one crystalline 1-(α-hydroxyethyl)-2-methylcyclohexanol (V), which indicates the selectivity of the reduction reaction. The analogous reduction of trans-ketol (VII) led to the isolation of liquid trans-1(α-hydroxyethyl)-2-methylcyclohexanol (VIII).



Glycols (V) and (VIII) gave, after partial acetylation, the corresponding monoacetates (VI) and (IX), among which the first was crystalline, the second – liquid.

In the Serini reaction with acetate (VI) (refluxing with zinc dust in o-xylene for six hours) there was formed trans-1-acetyl-2-methylcyclohexane (X), also prepared from the bromide of trans-hexahydro-o-toluic acid (XI) [3] and methylmagnesium iodide. The mixed melting point of semicarbazones of the two specimens showed no depression.



The Serini reaction with acetate (IX) gave a 43% yield of cis-1-acetyl-2-methylcyclohexane (XII), also obtained by the convergent synthesis from the chloride of cis-hexahydro-o-toluic acid (XIII) [3]. Besides the indicated ketones (X) and (XII) no other individual carbonyl compounds were detected among the products of the Serini reaction. This permits us to conclude that the Serini reaction proceeds stereospecifically with formation of a configurational inversion at the tertiary carbon atom, both in the cyclohexane series and in the steroid series.

EXPERIMENTAL

Ethyl-1-cyanocyclohexyl acetal [(II), R = H.] To the solution of 25 g of 1-cyanocyclohexanol [8] and 21.7 g of vinyl ethyl ether in 25 ml of absolute benzene there was added 10 drops of absolute ether saturated with hydrogen chloride. The mixture was cooled and left overnight, after which it was neutralized with solid caustic and distilled in vacuum. There was obtained 33.2 g of ethyl 1-cyanocyclohexyl acetal in the form of a colorless liquid.

B.p. 72-73° (2 mm), $n^{20}D$ 1.4480, d^{20}_4 0.9838. MR_D 53.71; calculated 53.90.
Found %: N 7.72, 7.83. $C_{11}H_{19}O_2N$. Calculated %: N 7.10.

Acetylcyclohexanol [(III), R = H]. To the Grignard reagent prepared from 15.6 g of methyl iodide and 2.7 g of magnesium in 70 ml of absolute ether there was added the solution of 19.7 g of ethyl 1-cyanocyclohexyl acetal in 20 ml of absolute ether. The mixture was refluxed with stirring for one hour; 60 ml of water was added with cooling along with 20 ml of concentrated hydrochloric acid, the mixture was stirred for one hour at 20° and was then neutralized with solid sodium bicarbonate. After the usual working-up and vacuum distillation, there was obtained 11.6 g of acetylcyclohexanol in the form of a colorless liquid with b.p. 58-61° (2.5 mm), $n^{20}D$ 1.4678 [9-12].

The semicarbazone had m.p. 198-199° (from methyl alcohol) and gave no depression in mixed melting point with semicarbazone prepared from the acetylcyclohexanol synthesized by hydration of 1-ethynylcyclohexanol.

Ethyl cis-1-cyano-2-methylcyclohexyl acetal [(II), R = CH_3]. From 27.8 g of cis-1-cyano-2-methylcyclohexanol [3] and 21.6 g of vinyl ethyl ether there was obtained, analogously to the above, 33.4 g of ethyl cis-1-cyano-2-methylcyclohexyl acetal in the form of a colorless liquid.

B.p. 80-81° (2.5 mm), $n^{20}D$ 1.4480, d^{20}_4 0.9720. MR_D 58.16; calculated 58.52.
Found %: N 6.62, 6.53. $C_{12}H_{21}O_2N$. Calculated %: N 6.58.

Cis-1-acetyl-2-methylcyclohexanol (IV). The reaction of 21.1 g of ethyl cis-1-cyano-2-methylcyclohexyl acetal with the Grignard reagent obtained from 15.6 g of methyl iodide and 2.7 g of magnesium was run under the conditions described above but with longer duration of the hydrolysis (two hours). After vacuum distillation there was isolated 5.5 g of 2-methylcyclohexanone with b.p. 50-56° (3 mm), $n^{20}D$ 1.4520. Semicarbazone (m.p. 189-191°) did not give a depression in mixed melting point with an authentic sample. There was obtained 8.3 g of cis-1-acetyl-2-methylcyclohexanol (IV) with b.p. 75-77° (3 mm), $n^{20}D$ 1.4720, m.p. 37-38° (from petroleum ether), which did not give a depression in mixed melting point with a specimen prepared by hydration of cis-1-ethynyl-2-methylcyclohexanol [4, 5, 12].

Semicarbazone of the ketol (IV) melted at 229-230° (from alcohol; with decomposition) and similarly did not give a depression in mixed melting point with an authentic sample [4, 5, 12].

Found %: N 19.98, 19.80. $C_{10}H_{19}ON_3$. Calculated %: N 19.71.

Ethyl trans-1-cyano-2-methylcyclohexyl acetal [(II), R = CH_3]. To the solution of 27.8 g of liquid mixture of cyanohydrins enriched with trans-1-cyano-2-methylcyclohexanol [3] and 21.6 g of vinyl ethyl ether in 25 ml of anhydrous benzene there was added 10 drops of ethereal solution of hydrogen chloride. The mixture was refluxed for 3.5 hours without access of moisture; it was then left overnight and then worked up as usual. There was obtained 31.7 g of a mixture of acetals with b.p. 82-89° (3 mm) from which by repeated distillation there was isolated ethyl trans-1-cyano-2-methylcyclohexyl acetal.

B.p. 84.5° (2.5 mm), $n^{20}D$ 1.4490, d^{20}_4 0.9686. MR_D 58.43; calculated 58.52.
Found %: N 6.98, 7.08. $C_{12}H_{21}O_2N$. Calculated %: N 6.68.

Trans-1-acetyl-2-methylcyclohexanol (VII). The above described mixture of acetals (21.1 g) entered into the reaction with the Grignard reagent prepared from 15.6 g of methyl iodide and 2.7 g of magnesium, as described above, with increased duration of hydrolysis to 3.5 hours. After the usual working-up and distillation there was obtained 4.5 g of 2-methyl-cyclohexanone with b.p. 50-55° (3 mm) and 5.9 g of a mixture of stereoisomeric 1-acetyl-2-methylcyclohexanols (IV) and (VII) with b.p. 64-77° (3 mm). By repeated fractional distillation there was isolated the trans-1-acetyl-2-methylcyclohexanol (VII) with b.p. 58-60° (2.5 mm), $n^{20}D$ 1.4655 [4], the semicarbazone of which melted at 218.5-219° (with decomposition) (from alcohol) and gave no depression in mixed melting point with an authentic sample prepared by hydration of trans-1-ethynyl-2-methylcyclohexanol [4, 5].

Found %: N 20.09, 20.08. $C_{10}H_{19}ON_3$. Calculated %: N 19.71.

When the acetals were introduced into the reaction without a preliminary purification, the yield of the ketols was raised by 5-10%.

Cis-1(α-hydroxyethyl)-2-methylcyclohexanol (V). A mixture of 15.6 g of cis-1-acetyl-2-methylcyclohexanol (IV) (m.p. 37-38°) and 270 g of 38% solution of aluminum isopropoxide in toluene was heated for four hours under a reflux condenser at 210°, after which 50 ml of anhydrous isopropyl alcohol was added and the azeotropic mixture with b.p. 70-80° was distilled until it gave a negative test for acetone. After the addition of 20 ml of additional isopropyl alcohol and refluxing for 1.5 hours, no more acetone was detected in the distillate. The reaction mixture was carefully stirred with 870 ml of 10% sulfuric acid, the toluene layer was separated while the aqueous layer was extracted three times with ether. After drying of the combined extracts with sodium sulfate, evaporation of the solvents and washing the residue with petroleum ether, there was obtained 12 g (76%) of cis-1(α-hydroxyethyl)-2-methylcyclohexanol (V) in the form of colorless needles with m.p. 94-94.5° (from a mixture of ether and petroleum ether).

Found %: C 68.52, 68.58; H 11.55, 11.53. $C_9H_{18}O_2$. Calculated %: C 68.29; H 11.47.

Acetate of cis-1(α-hydroxyethyl)-2-methylcyclohexanol (VI). The solution of 11.4 g of glycol (V) in 15 ml of pyridine and 8 g of acetic anhydride was kept for three days, after which it was acidified with dilute sulfuric acid and thoroughly extracted with ether. The ethereal extract was washed with bicarbonate solution, dried with sodium sulfate and, after the distillation of the solvent, yielded 14.2 g of the acetate of cis-1(α-hydroxyethyl)-2-methylcyclohexanol (XII) in the form of colorless crystals with m.p. 44-45° (from petroleum ether).

Found %: C 65.62, 65.83; H 10.02, 10.00. $C_{11}H_{20}O_3$. Calculated %: C 65.94; H 10.07.

Trans-1(α-hydroxyethyl)-2-methylcyclohexanol (VIII). Trans-1-acetyl-2-methylcyclohexanol (VII) (b.p. 82-83° at 10 mm, $n^{20}D$ 1.4620) (15.6 g) was reduced with 270 g of 38% solution of aluminum isopropoxide in toluene analogously to the above experiment. After distillation of the reaction products there was isolated 3.2 g of the starting ketol (VII) with b.p. 66-68° (4 mm), $n^{20}D$ 1.4610, and 8.2 g (52%) of trans-1(α-hydroxyethyl)-2-methylcyclohexanol (VIII) with b.p. 105° (6 mm), $n^{20}D$ 1.4880.

Found %: C 68.04, 68.07; H 11.38, 11.27. $C_9H_{18}O_2$. Calculated %: C 68.29; H 11.47.

Acetate of trans-1(α-hydroxyethyl)-2-methylcyclohexanol (IX). A solution of 7 g of trans-1(α-hydroxyethyl)-2-methylcyclohexanol (VIII) and 5.1 g of acetic anhydride in 4.4 g of pyridine was kept for two days and after the usual treatment yielded 7.8 g of the acetate of trans-1(α-hydroxyethyl)-2-methylcyclohexanol (IX) with b.p. 104.5° (4.5 mm), $n^{20}D$ 1.4672.

Found %: C 66.41; 66.32; H 9.91, 9.93. $C_{11}H_{20}O_3$. Calculated %: C 65.94; H 10.07.

Trans-1-acetyl-2-methylcyclohexane (X). a) A mixture of 150 g of activated zinc dust and 500 ml of anhydrous o-xylene was heated to boiling with agitation and part of the xylene was distilled off until all moisture had been removed. To the boiling mixture there was added 13 g of the acetate of cis-1(α-hydroxyethyl)-2-methylcyclohexanol (VI) and the mixture was refluxed with stirring for six hours with periodic distillation of acetic acid. The zinc dust was filtered off, washed with ether and the solvents were distilled in vacuum. After distillation of the product in vacuum there was obtained 5 g (52%) of trans-1-acetyl-2-methylcyclohexane (X) in the form of a colorless liquid with b.p. 49.5-51° (5 mm), $n^{20}D$ 1.4565.

The semicarbazone of trans-ketone (X) melted at 175-176° (from aqueous methyl alcohol) and did not give a depression in mixed melting point with an authentic sample. The mixed melting point with the semicarbazone of cis-ketone (XII) was 156-166°.

b) To the solution of 20.5 g of the bromide of trans-hexahydro-o-toluic acid (XI) [3] in 20 ml of absolute ether there was added the Grignard reagent prepared from 2.5 g of magnesium and 14.2 g of methyl iodide in 60 ml of ether, after which the product was hydrolyzed with dilute hydrochloric acid with cooling. By the usual working-up procedure there was isolated 5.6 g of trans-1-acetyl-2-methylcyclohexane (X) with b.p. 58-59° (7 mm), $n^{20}D$ 1.4548. The semicarbazone of the trans-ketone melted at 177-178° and gave no depression in mixed melting point with the above described specimens.

Found %: N 20.98, 21.01. $C_{10}H_{19}ON_3$. Calculated %: N 21.31. According to the literature data [13] the semicarbazone of the trans-ketone (XI) melts at 177-178.5°

Cis-1-acetyl-2-methylcyclohexane (XII). a) The Serini reaction was run as described above with 7 g of acetate (IX) and 100 g of activated zinc dust in 500 ml of absolute o-xylene. There was obtained 2.2 g of cis-1-acetyl-2-methylcyclohexane (XII) with b.p. 58-62° (7 mm), $n^{20}D$ 1.4665. The entire amount of the ketone (XII) was transformed into the semicarbazone which after several recrystallizations from aqueous methyl alcohol had m.p. 182-183° and did not give a depression in mixed melting point with an authentic sample. The mixed melting point with the semicarbazone of trans-ketone (X) (m.p. 177-178°) was 157-163°. After repeated fractional crystallization of the semicarbazone no other individual products could be isolated.

b) The cis-ketone (XII) was synthesized, as described above, from 24 g of the chloride of cis-hexahydro-o-toluic acid (XIII) [3] and the Grignard reagent prepared from 3.6 g of magnesium and 21.3 g of methyl iodide. After distillation there was obtained 9 g of cis-1-acetyl-2-methylcyclohexane (XII) with b.p. 58-62° (7.5 mm), whose semicarbazone melted at 182-183° and did not give a depression in mixed melting point with the preceding specimen.

Found %: N 21.22, 21.02. $C_{10}H_{19}ON_3$. Calculated %: N 21.31.

According to the literature data: semicarbazone of cis-ketone (XII) melts at 182-182.5° [13, 14].

SUMMARY

It was shown, with the example of stereoisomeric 1-(α-hydroxyethyl)-2-methylcyclohexanols, that the Serini reaction proceeds stereospecifically in the cyclohexane series and leads to inversion of configuration.

The reduction of cis-1-acetyl-2-methylcyclohexanol with aluminum isopropoxide also proceeds stereospecifically, yielding only one of the possible diols: 1-(α-hydroxyethyl)-2-methylcyclohexanol.

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THE SYNTHESIS OF MERCAPTOAMINO COMPOUNDS

III. SYNTHESIS OF 3-MERCAPTO-4-AMINO-2-METHYLBUTANE AND 5-AMINO-1-MERCAPTOPENTANE

Iu. V. Markova, L. N. Zenkova and M. N. Shchukina

The discovery of the protective action against radiation of β-mercaptoethylamine [1] stimulated interest in this class of compounds. In recent years there have been many papers in the literature on the investigation of different derivatives of β-mercaptoethylamine, chiefly its different salts, N^-, S^-, N and S substituted compounds, compounds with potential mercapto groups, aminoisothiuronium compounds, and others [2].

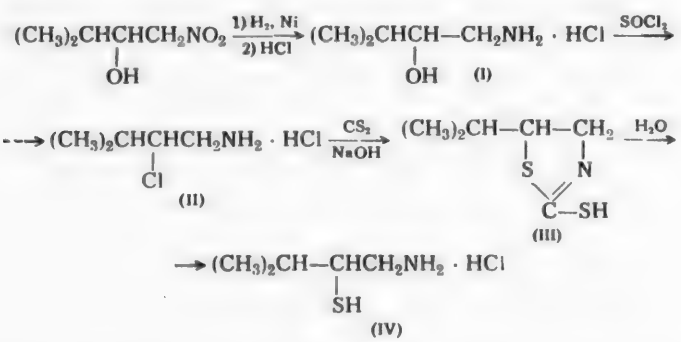
Homologs of β-mercaptoethylamine of the types $R-CH(SH)-CH_2NH_2 \cdot HCl$ and $HS(CH_2)_XNH_2 \cdot HCl$, have been almost unstudied.

It is therefore interesting to study the effect of length and nature of the alkyl chain and also the position of the functional groups by synthesizing a number of compounds of this type.

After we had completed this work, a study was published [3] in which this question received some consideration.

In the present work we have carried out the synthesis of the undescribed 3-mercapto-4-amino-2-methylbutane hydrochloride (IV) (Scheme 1) and 5-amino-1-mercaptopentane hydrochloride (VIII) (Scheme 2).

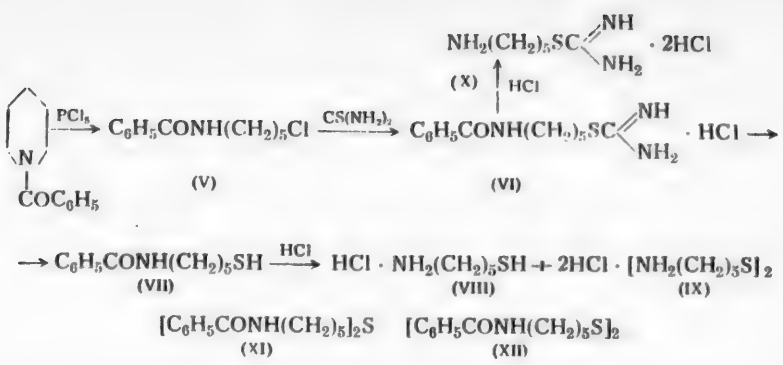
Scheme 1



3-Hydroxy-4-nitro-2-methylbutane, obtained by condensation of isobutyraldehyde with nitromethane [4], was reduced at room temperature in an autoclave in the presence of skeletal nickel to 3-hydroxy-4-amino-2-methylbutane (I), whose hydrochloride was converted to the corresponding chloride (II) by the action of thionyl chloride in dichloroethane. (II)and carbon disulfide gave 2-mercapto-5-isopropylthiazoline (III) which was hydrolyzed by concentrated hydrochloric acid at 160° to 3-mercapto-4-amino-2-methylbutane hydrochloride (IV).

In order to obtain 5-amino-1-mercaptopentane hydrochloride (VIII) from N-benzoylpiperidine, we prepared N-benzoyl-5-amino-1-chloropentane by the method of Braun [5]; the method was modified by simplifying

Scheme 2



the isolation and purification of the preparation and increasing the yield to 63%. (V) was converted by the action of thiourea to N-benzoyl-5-amino-1-isothiuroniumpentane hydrochloride (VI) which was heated with an alkaline solution to give N-benzoyl-5-amino-1-mercaptopentane (VII). (VII) was not formed from (VI) by the action of an alkaline solution at room temperature; it was transformed into the base N-benzoylamino-1-isothiuroniumpentane, from which (VII) could be obtained by further heating with an alkaline solution, or by the action of hydrochloric acid, the starting hydrochloride (VI) could be formed.

Hydrolysis of (VII) was carried out by heating with concentrated hydrochloric acid in a sealed tube at 140-150° for 5 hours, and also by boiling with 20% hydrochloric acid for 20-25 hours. As a result of the hydrolysis we obtained a crystalline substance which contained 70-72% 5-amino-1-mercaptopentane hydrochloride (VIII) and 28-30% of the dihydrochloride of the corresponding oxidized compound bis(5-aminopentyl)disulfide (IX). The presence of the hydrochloride (VIII) was established by iodometric titration, and the presence of the dihydrochloride (IX) was shown by analysis and acetylation of the obtained substance: when it was heated with acetyl chloride, by analogy with the preparation of S-acetylcysteamine hydrochloride [6] and other compounds of this type [7], it gave S-acetyl-5-amino-1-mercaptopentane hydrochloride, and we isolated bis(5-aminopentyl)disulfide dihydrochloride which was present in the starting material as an impurity.

Boiling (VI) with 20% hydrochloric acid for 8 hours gave an almost quantitative yield of 5-amino-1-isothiuronium dihydrochloride (X). When the latter was boiled with an equimolecular amount of alkali for 2 hours, and also when heated in a sealed tube at 140°, it gave a substance whose picrate had a m.p. 138-140° and whose formula was $C_6H_{15}N_3S \cdot C_6H_3O_7N_3$, that is, it corresponded to the starting amine. However, attempts to obtain from the picrate or directly from the reaction product the starting hydrochloride (X) gave no positive results. The structure of the substance was studied. Oxidation of (VII) with an alcoholic solution of iodine gave bis(N-benzoyl-5-aminopentyl) disulfide, and condensation of the same material with (V) in the presence of sodium alcoholate gave bis(N-benzoyl-5-aminopentyl)sulfide.

EXPERIMENTAL

3-Hydroxy-4-amino-2-methylbutane hydrochloride (I). To a solution of 17 g of 3-hydroxy-4-nitro-2-methylbutane [4] in 85 ml of ethyl alcohol was added 15 g of Raney nickel catalyst (paste) in alcohol. Hydrogenation was carried out at room temperature in an autoclave for 2 hours. After separation of the catalyst, the alcohol solution was acidified with hydrochloric acid and evaporated in a vacuum; the residue was recrystallized from alcohol. The yield was almost quantitative. M.p. 110° (decomp.) The literature [8] gives 110°.

3-Chloro-4-amino-2-methylbutane hydrochloride (II). To a suspension of 14 g of (I) in 100 ml of dry dichloroethane was added 13 g of thionyl chloride with stirring. The reaction mass was boiled 2 hours on the water bath, upon which the substance quickly dissolved, and then precipitated. After cooling, the precipitate was filtered, washed with dichloroethane, and dried in a vacuum desiccator. The yield of (II) was 14.8 g (92%). After recrystallization from alcohol, the substance had a melting point > 190°.

Found %: C 38.18; H 8.28; N 8.75; Cl 45.14. $C_5H_{13}NCl_2$. Calculated %: C 37.98; H 8.29; N 8.86; Cl 44.86.

2-Mercapto-5-isopropylthiazoline (III). To a solution of 5 g of (II) in 15 ml of water was added with stirring 10.5 ml of 24% sodium hydroxide solution and 2.4 g of carbon disulfide. The solution rapidly became yellow, then cloudy, and a precipitate came down; upon this the temperature rose to 40°. After the solution had been stirred for 30 minutes, it was acidified with hydrochloric acid and cooled, the precipitate was filtered off, washed with water, and dried in a vacuum desiccator. The yield of (III) was 3.4 g (80%). After recrystallization from alcohol it melted at 111-112°.

Found %: C 45.29; H 6.85; N 8.66; S 40.23. $C_6H_{11}NS_2$. Calculated %: C 44.70; H 6.87; N 8.73; S 39.70.

3-Mercapto-4-amino-2-methylbutane hydrochloride (IV). 1 g of (III) and 15 ml of concentrated hydrochloric acid were heated for 6 hours in a sealed tube at 160°. The reaction solution was evaporated to dryness in a vacuum; the residue was dissolved in anhydrous alcohol. After addition of anhydrous ether to the alcohol solution to cloudiness, the precipitate was filtered, and washed with ether. We obtained 0.8 g of (IV). M.p. 214-218° (decomp.) According to iodometric titration, the substance contained 95% (IV).

Found %: C 38.43; H 8.91; N 8.48; S 20.19; Cl 22.84. $C_5H_{14}NSCl$. Calculated %: C 38.56; H 9.06; N 8.70; S 20.59; Cl 22.74.

N-Benzoyl-5-amino-1-chloropentane (V). A mixture of 935 g of N-benzoylpiperidine and 105 g of phosphorus pentachloride was carefully heated until reaction began, after which it was boiled 30-40 minutes to the formation of a homogeneous solution. After it had cooled, the reaction solution was poured with stirring over cracked ice; the substance then precipitated in the form of an oil which crystallized with further stirring; it was neutralized by grinding with a cold 40% solution of sodium hydroxide, filtered, and washed with ice water and petroleum ether. The yield of (V) was 70 g (62.6%). After recrystallization from alcohol, it melted at 64-65°. According to the literature [5] the m.p. is 66°.

N-Benzoyl-5-amino-1-isothiuronium pentane hydrochloride (VI). 22.6 g of (V), 7.6 g of thiourea, and 60 ml of anhydrous alcohol were refluxed for 6 hours. The precipitate which separated on cooling was filtered off and washed with alcohol and ether. We obtained 17 g of (VI). M.p. 174-176°. After the mother liquors had been evaporated in a vacuum and cooled they yielded 3 more g of (VI). The total yield was 66.2%. After recrystallization from alcohol the substance melted at 180-181.5°. It was difficultly soluble in cold water and cold alcohol.

Found %: C 51.92; H 6.90; N 13.57; S 10.62; Cl 12.14. $C_{13}H_{20}N_2SCl$. Calculated %: C 51.73; H 6.68; N 13.92; S 10.62; Cl 11.75.

The base of this compound was obtained from (VI) by treatment with alkali at room temperature. The compound crystallized with one molecule of water. M.p. 105-107° (from alcohol).

Found %: N 14.84; S 11.23. $C_{13}H_{19}ON_2S \cdot H_2O$. Calculated %: N 14.82; S 11.31.

N-Benzoyl-5-amino-1-mercaptopentane (VII). To a solution of 20 g of N-benzoyl-5-amino-1-isothiuronium pentane hydrochloride in 300 ml of water was added 22 ml of 12% sodium hydroxide. The reaction mass was boiled for 10 minutes. The substance quickly dissolved, then an oil precipitated, which crystallized on cooling. The precipitate was filtered, washed with water, and dried in a vacuum desiccator. The yield of (VII) was 14 g (95.3%). M.p. 72-75°. After recrystallization from 70% alcohol it melted at 76-77°.

Found %: C 64.66; H 7.52; N 6.23; S 14.70; SH 14.70. $C_{12}H_{17}ONS$. Calculated %: C 64.53; H 7.67; N 6.27; S 14.35; SH 14.80.

Bis(N-benzoyl-5-aminopentyl)disulfide (XII). To a solution of 4 g of (VII) in 50 ml of alcohol was added a 2% alcoholic solution of iodine until a yellow color appeared. The resulting precipitate was filtered and recrystallized from alcohol. The yield of (XII) was 3.5 g (87.5%). M.p. 133-135°. According to the literature [9] it melts at 132-133°.

Bis(N-benzoyl-5-aminopentyl)sulfide (XI). To 0.23 g of metallic sodium in 20 ml of anhydrous alcohol was added with stirring 2.23 g of (VII) and then 2.25 g of (V), after which the reaction mixture was boiled for 1.5 hours. The resulting precipitate was filtered, washed with water, and dried in a vacuum desiccator. The yield was almost quantitative. After recrystallization from alcohol the substance melted at 94-95°. According to the literature [9] the m.p. is 96°.

5-Amino-1-mercaptopentane hydrochloride (VIII) and its disulfide (IX). 5 g of (VII) and 25 ml of concentrated hydrochloric acid were heated in a sealed tube at 140° for 5 hours. The benzoic acid which precipitated was filtered off, and the filtrate, after addition to it of 100 ml of water, was evaporated in a vacuum to dryness. The crystalline residue was dried in a vacuum desiccator over P_2O_5. The yield of (VIII) was 3.2 g. M.p. 95-105°. The substance contained 70-72% (VIII). Due to its hygroscopic nature the substance was analyzed without further purification.

Found %: C 38.80; H 8.75; N 6.86. $C_5H_{14}NSCl$. Calculated %: C 38.56; H 9.06; N 9.05.

X-Acetyl-5-amino-1-mercaptopentane hydrochloride. 1 g of (VIII) and (IX) from the previous experiment and 5 ml of acetyl chloride were heated on a water bath at 40° for 30 minutes. At the end of the heating the insoluble precipitate was filtered off and the solution was cooled with ice water. The acetyl derivative which precipitated was filtered, washed with absolute ether, and dried over phosphorus pentoxide in a vacuum desiccator. The yield of acetyl compound was 0.6 g. M.p. 125-130°.

Found %: C 42.33; H 8.23; N 7.70; S 16.60; Cl 17.97. $C_7H_{16}ONSCl$. Calculated %: C 42.52; H 8.15; N 7.79; S 16.21; Cl 17.93.

The insoluble precipitate which was filtered off after heating with acetyl chloride was recrystallized from alcohol with ether. It was compound (IX). A mixed melting point with the same substance obtained by hydrolysis of compound (XII) with hydrochloric acid [9] gave no depression. M.p. 225-235° (decomp). According to the literature [10] the melting point is 230°.

Found %: C 38.80; H 8.42; N 8.55; Cl 22.80. $C_{10}H_{26}N_2S_2Cl_2$. Calculated %: C 38.83; H 8.47; N 9.05; Cl 22.92.

5-Amino-1-isothiuronium pentane dihydrochloride (X). 30.2 g of (VI) and 300 ml of 20% hydrochloric acid were refluxed for 8 hours. The benzoic acid which precipitated on cooling was filtered off, and the filtrate was evaporated to dryness in a vacuum. The residue was dissolved in anhydrous alcohol. After addition of ether the solution gave a precipitate which was filtered and washed with ether. The yield of (X) was 19.8 g (84.6%). M.p. 141-143°.

Found %: C 30.46; H 6.96; N 17.59; S 13.55; Cl 30.44. $C_6H_{17}N_3SCl_2$. Calculated %: C 30.76; H 7.13; N 17.98; S 13.69; Cl 30.28.

SUMMARY

1. We have carried out the synthesis of 3-mercapto-4-amino-2-methylbutane hydrochloride and 5-amino-1-mercaptopentane and its acetyl derivative.

2. We have shown that in the hydrolysis of N-benzoyl-5-amino-1-mercaptopentane by hydrochloric acid, along with the formation of 5-amino-1-mercaptopentane hydrochloride, there is partial oxidation of the latter to the corresponding disulfide.

3. From N-benzoyl-5-amino-1-isothiuronium pentane dihydrochloride by acid hydrolysis we have obtained 5-amino-1-isothiuronium pentane dihydrochloride which is not hydrolyzed by heating with alkali.

4. In the oxidation of N-benzoyl-5-amino-1-mercaptopentane by alcoholic iodine we have obtained bis(N-benzoyl-5-aminopentyl)-disulfide, and by condensation of the same starting material with N-benzoyl-5-amino-1-chloropentane, bis(N-benzoyl-5-aminopentyl)sulfide.

5. We have worked out a satisfactory process for obtaining N-benzoyl-5-amino-1-chloropentane with a yield of 63%.

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THE REACTION OF DINITRODIOLEFINS WITH COMPOUNDS WHICH CONTAIN MOBILE HYDROGEN IN METHYLENE GROUPS*

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The chemistry of unsaturated nitrocompounds has developed almost entirely in the direction of seeking effective methods of synthesis and studies of the transformations of aliphatic, aromatic, and heterocyclic mononitroolefins. Great progress has been made in this field [1-4].

Up to now, compounds which contain two nitro groups have been little studied. It is only known that some of them combine with ammonia, aniline, bromine [5, 6], and mercaptans [7], and after condensation with phenylnitromethane and p-bromophenylnitromethane they are converted into isoxazoline oxides [5]. It has also been shown that dinitrodiolefins obtained by condensation of terephthalic aldehyde with nitromethane have an increased antibacterial activity [8].

In this connection it is important to study methods of synthesis of some dinitrodiolefins, derivatives of terephthalic aldehyde, and their reactions with compounds which contain mobile hydrogen atoms in the methylene group.

When ethylenediamine is used as a catalyst [9] and the usual method of condensation of terephthalic aldehyde with nitromethane is changed [5, 10], it is possible in special cases to increase considerably the yield of dinitrodiolefins (Table 1).

TABLE 1

Obtaining Dinitrodiolefins

Substance	Dinitrodiolefin	Catalyst	Yield (in %)	Literature data: catalyst	Literature data: yield (in %)
(I)	$O_2NHC{=}HC{-}C_6H_4{-}CH{=}CHNO_2$	Sodium hydroxide	67	Sodium hydroxide	* [10]
(II)	$O_2N{-}C(CH_3){=}HC{-}C_6H_4{-}CH{=}C(CH_3){-}NO_2$	Ethylenediamine	47	n-Butylamine	31 [8]
				n-Amylamine	43 [5]
(III)	$O_2N{-}C(C_6H_5){=}HC{-}C_6H_4{-}CH{=}C(C_6H_5){-}NO_2$	Ethylenediamine	46		

*The yield is not given in this work; according to our experiments, it is 5-6%.

The dinitrodiolefins which were obtained were reacted with a series of substances which contained mobile hydrogen atoms in the methylene group: malonic and acetoacetic esters, phenylmethylpyrazolone, cyanoacetic and nitroacetic esters, and phenylnitromethane.

*Previous communication, see J. Gen. Chem. 28, 675 (1958).

In the nitroolefins which we used, the nitro groups at opposite ends of the molecule caused different behavior in the conjugated systems. This increased the interest in the study, since the question of the reactivity of nitrocompounds with such structures is still open.

First of all, and in greatest detail, we studied 1,4-bis(β-nitrovinyl)benzene (I).

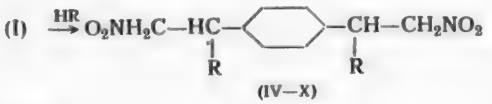
Attempts to combine diethyl malonate with this dinitrodiolefin in the presence of organic bases did not give positive results. However, its reaction with sodium malonic ester in anhydrous ethanol or methanol was carried out successfully with the formation of the ethyl (IV) and methyl esters (V) of the condensation product. In methanol solution under the influence of sodium methylate there first occurred transesterification of diethyl malonate [11], and then reaction of the sodium dimethyl malonate which was formed with the dinitrodiolefin(I); the condensation product in this case did not undergo any transesterification.

Condensation of cyanoacetic ester with the dinitrodiolefin(I) under the catalytic influence of triethylamine [12] proceded very easily even in the cold, but the isolation and purification of reaction product (VI) was very difficult; this difficulty was removed when triethyl amine was replaced by sodium methylate.

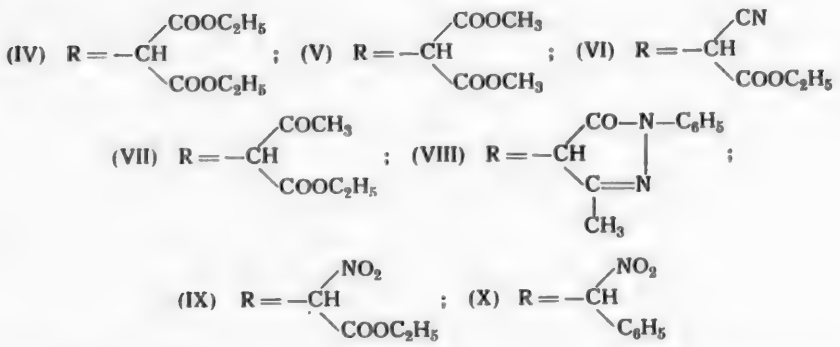
Acetoacetic ester in the presence of pyridine, piperidine, and dimethylaniline did not react with dinitrodiolefin(I). The expected condensation product (VII) was obtained in 83% yield after short boiling of the starting substance in methanol solution in the presence of triethylamine.

Under the catalytic influence of triethylamine the dinitrodiolefin(I) reacts very easily with phenylmethylpyrazolone, forming a high yield of product (VIII).

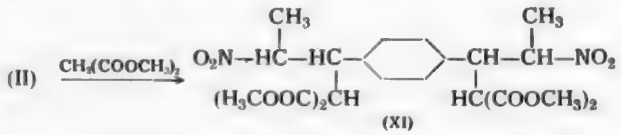
The use of triethylamine also permitted us to carry out the combination with the dinitrodiolefin (I) of nitroacetic ester and phenylnitromethane, as a result of which reactions we synthesized products (IX) and (X).



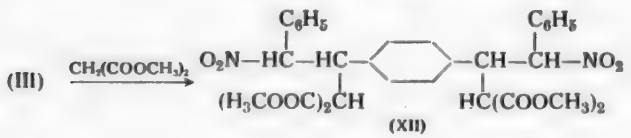
(IV–X)



To determine the reactivity of other dinitrodiolefins, we carried out the condensation of 1,4-bis(β-methyl-β-nitrovinyl)benzene (II) and 1,4-bis(β-phenyl-β-nitrovinyl)benzene (III) with sodium dimethyl malonate, completing the synthesis of the products (XI) and (XII).



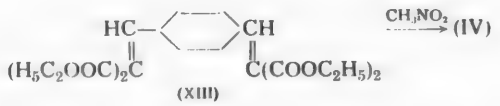
(XI)



(XII)

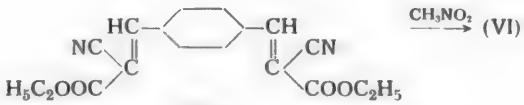
The dinitrodiolefins (I) and (II) easily combine with sodium dimethyl malonate at temperatures to 10°; dinitrodiolefin (III) under these conditions does not react, but at higher temperatures up to 50° it condenses successfully. Evidently among the studied dinitrodiolefins, (III) is the least active, probably for steric reasons caused by the benzene ring at the double bonds.

We devoted much attention to determining the structures of the reaction products from the dinitrodiolefins and the methylene compounds; this problem was solved by different synthesis. Thus, in the reaction of nitromethane with 1,4-bis(β,β-dicarbethoxyvinyl)benzene (XIII), specially obtained for this purpose from condensation of terephthalic aldehyde with malonic ester [13], we obtained a substance identical with (IV).



(XIII)

In a similar way we established the structure of the reaction product from dinitrodiolefin (I) and cyanoacetic ester: 1,4-bis(β-carbethoxy-β-cyanovinyl)benzene (XIV) condensed with nitromethane to form a compound identical with (VI).



(XIV)

When product (VII) was heated with phenylhydrazine in the presence of sodium bisulfite [14] in ethanol solution, we obtained a phenylmethylpyrazolone derivative identical with the reaction product from dinitrodiolefin (I) and phenylmethylpyrazolone (VIII).

Second synthesis confirmed the structure of the condensation products of 1,4-bis(β-nitrovinyl)benzene with malonic, acetoacetic, and cyanoacetic esters, and phenylmethylpyrazolone, and also made it possible to judge the structures of substances synthesized in a similar way: by the reaction of the dinitrodiolefin (I) with nitroacetic ester and phenylnitromethane, and the diolefins (II) and (III) with malonic ester.

It is important to remark that the studied dinitrodiolefins are more stable to polymerization than are the mononitroolefins of the benzene series. This makes it possible to carry out a number of syntheses (reactions with nitro- and cyanoacetic esters) with greater success than in the case of the mononitroolefins.

We should point out that the dinitrodiolefins react with two moles of the methylene component. It follows from this that with two opposite possible directions for the conjugated system, there is nothing to prevent the condensation of these dinitrodiolefins at both double bonds.

EXPERIMENTAL

1,4-Bis(β-nitrovinyl)benzene (I). In a three-necked flask was placed 10.7 g of terephthalic aldehyde, 60 ml of methanol, and 10 g of nitromethane, and after it was cooled to −5°, a cold solution of 12.8 g of sodium hydroxide in 20 ml of water was added over 10-15 seconds with energetic stirring; the temperature of the reaction mass rose to 40-45°. The thick, snow white suspension was cooled to 5° and kept at this temperature for 10 minutes, then 120 ml of ice water was added. After several minutes an almost colorless solution formed; it was poured with stirring and cooling into 160 ml of 4 N hydrochloric acid. The resulting precipitate of dinitrodiolefin (I) was filtered, washed with water, sucked dry and dissolved in the minimum amount of boiling acetone; hot ethanol was added to cloudiness and the solution left for crystallization. On the next day we obtained 9 g of large golden needles with m.p. 231-232° (decomp). A test sample of (I) with the dinitrodiolefin synthesized according to Thiele [10] (with exact agreement with his yield of 5-6%) gave no depression of melting point. When the solvent was partly distilled from the residue a further 2.8 g of product with m. p. 229-231° (decomp.) was formed. Total yield 11.8 g (67%).

1,4-Bis(β-methyl-β-nitrovinyl)benzene (II). A solution of 1.34 g of terephthalic aldehyde, 4 g of nitroethane, 2 ml of alcohol and 2 drops of ethylenediamine was kept for 23-25 days at 28-30° in a sealed tube with periodic shaking. The light yellow needles of dinitrodiolefin(II) were filtered off, washed with alcohol, then with ether; m.p. 122-123° (from ethanol). Yield 1.17 g (47%).

1,4-Bis(β-phenyl-β-nitrovinyl)benzene (III). A solution of 1.34 g of terephthalic aldehyde, 2.74 g of phenylnitromethane, 3 ml of benzene and a drop of ethylenediamine was heated 16 hours in a thermostat at 60-65°. The resulting light yellow crystalline precipitate of dinitrodiolefin(III) was filtered, and washed with alcohol; m.p. 229° (decomp.) (from acetone). Yield 1.71 g (46%).

1,4-Bis(α-nitromethyl-β,β-dicarbethoxyethyl)benzene (IV). To a suspension of 1.1 g of 1,4-bis(β-nitrovinyl)benzene in 5 ml of anhydrous ethanol, cooled to −2°, was added over several minutes with good stirring sodium malonic ester prepared by dissolving 0.23 g of metallic sodium in a mixture of 1.8 g of diethyl malonate and 5 ml of anhydrous ethanol. The reaction mass was stirred for 1.5 hours at 2° and then the thick suspension was gradually treated with 20 ml of ethanol and 0.9 g of glacial acetic acid and the colorless precipitate was filtered. Yield 1.95 g (72%).

Colorless crystals with m.p. 158-160° (from a mixture of ethanol and acetone); the product was easily soluble in acetone, not soluble in water or ethanol.

Found %: C 52.88, 52.84; H 6.10, 6.07; N 5.07, 5.14. $C_{24}H_{32}O_{12}N_2$. Calculated %: C 53.33; H 5.96; N 5.18.

1,4-Bis(α-nitromethyl-β,β-dicarbomethoxyethyl)benzene (V). To a suspension of 2.2 g of 1,4-bis(β-nitrovinyl)benzene in 20 ml of anhydrous methanol at 0-5° was gradually added sodium malonic ester, prepared from a solution of 0.46 g of metallic sodium in a mixture of 4 g of diethyl malonate and 5 ml of anhydrous methanol. After 1.5 hours stirring at 0°, 1.5 ml of glacial acetic acid was added by drops to the clear solution; the colorless precipitate was stirred for 1 hour, then filtered and washed with ethanol. Yield 3.7 g (72%). M.p. 161-163° (repeatedly crystallized from a mixture of benzene and acetone). The product was easily soluble in benzene and acetone, not soluble in methanol and ethanol.

Found %: C 49.60, 49.75; H 5.12, 5.60; N 5.96, 6.14. $C_{20}H_{24}O_{12}N_2$. Calculated %: C 49.58; H 4.99; N 5.78.

1,4-Bis(α-nitromethyl-β-carbethoxy-β-cyanoethyl)benzene (VI). To a suspension of 1.1 g of 1,4-bis(β-nitrovinyl)benzene, and 1.15 g of ethyl cyanoacetate in 10 ml of anhydrous methanol, cooled to −5°, was added over 5 minutes at a temperature not above 0°, a solution of sodium methylate prepared by dissolving 0.23 g of metallic sodium in 7 ml of anhydrous methanol.

The reaction mass was stirred for 20-30 minutes with cooling, and the resulting clear solution was treated with 0.8 ml of glacial acetic acid, added by drops over 0.5 hour. For full separation of the condensation product, the reaction mass was kept for 4-6 hours at 0-5° in a refrigerator. The heavy precipitate was filtered and washed with methanol.

Colorless crystals with m.p. 170-171° (from acetone with later addition of methanol); soluble in acetone and ethyl acetate, not soluble in benzene and chloroform. Yield 1.7 g (76%).

Found %: N 12.59, 12.46. $C_{20}H_{22}O_8N_4$. Calculated %: N 12.55.

1,4-Bis(α-nitromethyl-β-acetyl-β-carbethoxyethyl)benzene (VII). A mixture of 0.44 g of 1,4-bis(β-nitrovinyl)benzene, 0.65 g of acetoacetic ester, 5 ml of methanol and 2 drops of triethylamine was boiled 20 minutes on the water bath, then heating was stopped and after 3 hours the snow white precipitate was filtered off. M.p. 185-186° (boiled in ethanol), not soluble in water and alcohol, soluble in heated dioxane, acetone, benzene. Yield 0.8 g (86%).

Found %: N 5.85, 5.88. $C_{22}H_{28}O_{10}N_2$. Calculated %: N 5.83.

1,4-Bis[α-4-(1-phenyl-3-methylpyrazolonyl)-β-nitroethyl] benzene (VIII). A mixture of 0.5 g of 1,4-bis(β-nitrovinyl)benzene and 0.9 g of 1-phenyl-3-methyl-5-pyrazolone in 50 ml of methanol was boiled for several minutes on the water bath until solution resulted. Then heating was stopped and 2 drops of triethylamine

were added to the reaction mass. After 30 minutes, the slightly colored precipitate of the condensation product was filtered from the still warm solution. Washing the precipitate with hot methanol gave a product with m.p. 246-247° (decomp). Yield 1.1 g (85%).

The slightly colored crystalline product with m.p. 246-247° (from warmed methanol) dissolved easily in mineral acids and alkalis and pyridine, and with more difficulty in boiling glacial acetic acid; it was not soluble in the usual organic solvents.

Found %: C 63.37, 63.33; H 5.44, 5.55. $C_{30}H_{28}O_6N_6$. Calculated %: C 63.37; H 4.96.

1,4-Bis(α-nitromethyl-β-nitro-β-carbethoxyethyl)benzene (IX). A mixture of 0.44 g 1,4-bis(β-nitrovinyl) benzene and 0.72 g of nitroacetic ester in 5 ml of acetone was heated for several minutes on the water bath. After addition of one drop of triethylamine to the suspension, cooled to 50°, a red solution slowly formed and was stirred for an hour more while it cooled by itself. The oily residue after evaporation of the acetone was mixed with 8-10 ml of methanol. The precipitate which separated after several hours was mixed with ether, filtered, and washed with methanol and then ether.

Colorless, transparent needles with m.p. 171-173° (repeatedly crystallized from a mixture of acetone and ethanol); easily soluble in benzene and acetone, insoluble in ethanol and water. Yield 1 g (quantitative).

Found %: C 44.54, 44.79; H 4.85, 5.05; N 11.58, 11.67. $C_{18}H_{22}O_{12}N_4$. Calculated %: C 44.55; H 4.56; N 11.52.

1,4-Bis(α-nitromethyl-β-nitro-β-phenylethyl)benzene (X). To a suspension of 1.1 g of 1,4-bis(β-nitrovinyl)-benzene in a mixture of 1.37 g of phenylnitromethane and 10 ml of methanol at 50-60° was added 2 drops of triethylamine; a heavy, colorless precipitate slowly formed. The reaction mass was boiled for 5 minutes to complete the reaction, then it was cooled and the condensation product was filtered and washed with methanol.

Fine colorless needles with m.p. 219-222° (decomp.) (from acetone with later addition of ethanol); easily soluble in acetone, dioxane, and pyridine; insoluble in methanol, ethanol, benzene, chloroform, and xylene. Yield 2.1 g (85%).

Found %: C 58.21, 58.15; H 4.41, 4.63; N 11.25, 11.69. $C_{24}H_{22}O_8N_4$. Calculated %: C 58.30; H 4.48; N 11.33.

1,4-Bis(α,α-dicarbomethoxymethyl-β-nitropropyl)benzene (XI). To a suspension of 1.24 g of 1,4-bis (β-methyl-β-nitrovinyl)benzene in 7 ml of anhydrous methanol cooled to 0° was gradually added at temperatures not exceeding 5° a solution of sodium malonic ester prepared by dissolving 0.23 g of metallic sodium in a mixture of 2 g of diethyl malonate and 8 ml of anhydrous methanol. Soon after the addition of malonate a clear solution formed, and from it with stirring at 8-10° there gradually formed a heavy precipitate of the sodium salt of the condensation product; after 30 minutes the reaction mass was dissolved by addition of 15 ml of water; 0.1 g of active charcoal was stirred in for 15 minutes at 10-15° and was then filtered off. The colorless filtrate was cooled to 5° and gradually acidified with 1 ml of glacial acetic acid. After 1 hour the snow white precipitate of the condensation product was filtered off and washed with a small amount of methanol and then with water. Fine colorless needles with m.p. 182-183° (from aqueous methanol); easily soluble in the cold in acetone, glacial acetic acid, and hot methanol. Yield 2.35 g (91%).

Found %: C 51.84, 51.58; H 5.73, 5.71; N 5.52, 5.24. $C_{22}H_{28}O_{12}N_2$. Calculated %: C 51.56; H 5.50; N 5.47.

1,4-Bis(α,α-dicarbomethoxymethyl-β-nitro-β-phenylethyl)benzene (XII). To a suspension of 1.11 g of 1,4-bis(β-nitro-β-phenylvinyl)benzene in 5 ml of anhydrous methanol at 15-20° was added a solution of sodium malonic ester, prepared by dissolving 0.14 g of metallic sodium in a mixture of 1.0 g of diethyl malonate and 5 ml of anhydrous methanol. The reaction mass was heated for 30 minutes with stirring to 50° and kept at this temperature for 1 hour. Complete solution of the starting dinitrodiolefin indicated the end of the reaction. The clear solution was cooled to room temperature and acidified with 0.5 g of glacial acetic acid. On the next day the precipitate of the condensation product was filtered and washed with methanol. Yield 1.4 g (73%). Colorless crystalline product with m.p. 193-196° (from a mixture of benzene and methanol); easily soluble in benzene, chloroform, and dichloroethane; more difficultly in acetone, insoluble in methanol.

Found %: C 60.42, 60.30; H 5.29, 5.54; N 4.39, 4.41. $C_{32}H_{32}O_{12}N_4$. Calculated %: C 60.37; H 5.06; N 4.40.

1,4-Bis(β,β-dicarbethoxyvinyl)benzene (XIII). A mixture of 2 g of terephthalic aldehyde and 6.4 g of diethyl malonate was heated 20 hours on the boiling water bath in a flask fitted with a reflux condenser and a calcium chloride tube. Each hour after beginning the heating 1 drop of piperidine was added; then the reaction mass was diluted with 20-25 ml of ethanol and the mixture boiled until the precipitate dissolved. The hot solution was filtered from the slight amount of insoluble precipitate and allowed to stand for crystallization. Yield 4.5 g (72%). The colorless crystalline product with m.p. 136-137° (from ethanol) was easily soluble in acetone, hot methanol, and ethanol.

Found %: C 63.25, 63.10; H 6.48, 6.23. $C_{22}H_{26}O_8$. Calculated %: C 63.14; H 6.26.

1,4-Bis(α-nitromethyl-β,β-dicarbethoxyethyl)benzene (IV). To a solution of sodium methylate, prepared by dissolving 0.14 g of metallic sodium in 10 ml of anhydrous methanol 0-5°, was added 1.8 g of nitromethane, then 1.26 g of 1,4-bis(β,β-dicarbethoxyvinyl)benzene. The suspension was stirred for 2 hours with the temperature constantly rising to a final value of 25°, at which time a clear solution of the sodium salt of the condensation product had formed. The solution was cooled to 10° and 0.6 g of glacial acetic acid was slowly added. After 30 minutes the resulting precipitate was filtered and washed with methanol. The product had a m.p. of 158-159° (from a mixture of ethanol and acetone); a mixed m.p. with a sample of(IV)gave no depression. Yield 0.7 g (42%).

1,4-Bis(β-carbethoxy-β-cyanovinyl)benzene (XIV). To a mixture of 1.34 g (0.01 g-mole) of terephthalic aldehyde, 2.3 g of ethyl cyanoacetate and 40 ml of ethanol was added 1 drop of piperidine with stirring at 20-25°. A clear solution slowly formed, and from it a crystalline condensation product gradually precipitated; it was filtered after 10 hours and washed with methanol. Yield 3.14 g (96%). Yellow-green needles with m.p. 198-199° (from toluene); soluble in hot benzene, acetone, and insoluble in ethanol.

Found %: C 66.58, 66.28; H 5.30, 5.51. $C_{18}H_{16}O_4N_2$. Calculated %: C 66.66; H 4.97.

1,4-Bis(α-nitromethyl-β-carbethoxy-β-cyanoethyl)benzene (VI). To a solution of sodium methylate, prepared by dissolving 0.23 g of metallic sodium in 20 ml of anhydrous methanol at 0°, was added 1.5 ml of nitromethane, then in one lot 1.62 g of 1,4-bis(β-carbethoxy-β-cyanovinyl)benzene (XIV). The suspension was stirred 1 hour at 0-2° until a solution was formed, and this was treated at the same temperature over 0.5 hour with 1 ml of glacial acetic acid. At the end of the addition of acid, precipitation began and the colorless precipitate of the condensation product was stirred for 1 hour with cooling, filtered, and washed with methanol. Yield 1.85 g (83%). M.p. 170-171° (twice crystallized from acetone with later addition of methanol). A mixed m.p. with the product(VI)gave no depression.

1,4-Bis[α-4-(1-phenyl-3-methylpyrazolonyl)-β-nitroethyl]benzene (VIII). A mixture of 1.2 g of 1,4-bis-(α-nitromethyl-β-acetyl-β-carbethoxyethyl)benzene (VII), 0.54 g of phenylhydrazine and 3 drops of a solution of sodium bisulfite in 10 ml of ethanol was boiled for 1 hour. After the solution had cooled, the precipitate was filtered and washed with ethanol. The product had a m.p. of 250° (decomp.) (from glacial acetic acid). A mixed m.p. with(VIII)gave no depression.

SUMMARY

1. We have shown that aromatic dinitrodiolefins in the presence of basic catalysts condense with substances which contain a mobile hydrogen atom in the methylene group.

2. We have shown that the presence in the dinitrodiolefins of two oppositely directed conjugated systems does not hinder the condensation process with active methylene components when two nitrovinyl groups take part.

3. The lowest activity of the 1,4-bis(β-phenyl-β-nitrovinyl)benzene among the three nitroolefins which we studied is evidently connected with steric hindrance by the phenyl nucleus on the double bonds.

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A STUDY OF IONO-CATALYTIC TELOMERIZATION

I. TELOMERIZATION OF ISOPRENE WITH ITS HYDROCHLORIDE

K. V. Leets

It was first reported in a patent [1] that it was possible to combine an alkyl halide with a diene hydrocarbon in the presence of ionic catalysts, zinc or tin halides.

Later [2-4] it was shown that this reaction has the character of a telomerization and the formation of one or another reaction product depends on the nature of the starting substance.

With isoprene as an example [3, 5] it was established that the first product of combination of an alkyl halide with isoprene could be obtained in considerable yield only if the telomerization reaction is cut short, stopping the action of the catalyst before 50% of the halogen compound has reacted. These conditions permit the use of the telomerization reaction for carrying out a very simple synthesis of citral from isoprene [6]. In recent work it has been shown that in the telomerization of isoprene with its hydrochloride a mixture of geranyl chloride, isomeric monoterpene chlorides (chiefly terpenyl chloride) and polyterpene chlorides is formed.

In the present paper we give experimental data and theoretical ideas of the author, which prove the importance of the moment of stopping the reaction as one of the main factors which affects the composition of the telomerization products of halogen compounds with dienes.

In this work we have studied the change in composition of the products of telomerization of isoprene with its hydrochloride depending on the intensity of the reaction.*

For the study we used a mixture of isoprene with its hydrochloride obtained by treating isoprene with gaseous hydrogen chloride. [7]. Methylene chloride was the solvent and anhydrous tin chloride was the catalyst. The degree of transformation could be determined by its dependence on the specific gravity of the reaction mixture. The reaction was stopped by removing the catalyst from the reaction mixture with water. The telomer which was obtained was distilled in a vacuum into fractions of monoterpene and polyterpene chlorides, and geranyl chloride was determined in the terpene chlorides by combining it with urotropine [6].

In Figure 1 we give the relation of composition of telomerization products to intensity of reaction, in Fig. 2, the relation of yield of geranyl chloride to the same factor.

As Fig. 1 shows, in the initial stages of the telomerization reaction, the content of all the transformation products in the mixture increases simultaneously, and then begins a rapid growth in content of polyterpene ch-chlorides and a cessation of growth of geranyl chloride. In the final stages of the process the geranyl chloride content falls, at the end of the reaction almost reaching zero. The increase in monoterpene chlorides (terpenyl chloride) is almost constant and only falls at the end of the reaction.

Figure 2 shows that the yield of geranyl chloride is inversely proportional to the intensity of the reaction. Thus, to get a higher yield of geranyl chloride it is necessary to break off the reaction of telomerization at a low intensity.

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*By intensity of the reaction we mean the degree of use of bound and free isoprene, or, in other words, the degree of transformation of isoprene and the hydrochloride into the telomer.

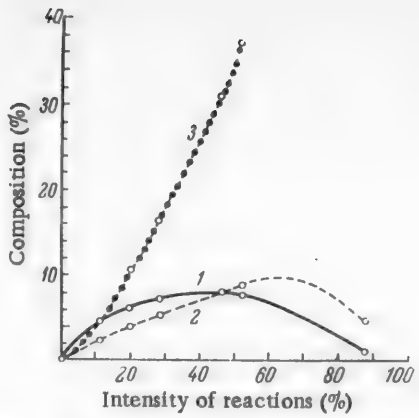

Fig. 1. Composition of telomerization products depending on intensity of reaction. 1) Geranyl chloride; 2) isomeric terpene chlorides; 3) polyterpene chlorides.

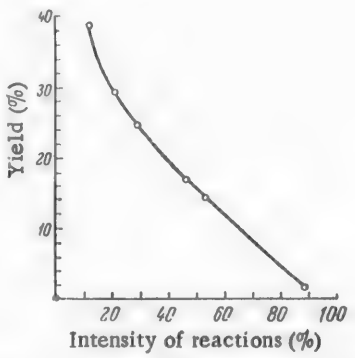

Fig. 2. Yield of geranyl chloride from isoprene (free and bound) which enters the reaction.

This effect can easily be explained on the basis of the earlier ideas [3, 4] of the existence of two kinetic stages in the reaction of combination of halogen derivatives and diene hydrocarbons under the influence of ionic catalysts. As we have shown, the yield of primary combination product depends on the ratio of reactivities of the initial and formed halogen compounds; the primary product can be separated only if the rate of the further reaction with the diene hydrocarbon is less than the rate of its formation. In the case studied, judging by the structure and the mobility of the halogen atom, the corresponding reactivity of the isoprene hydrochloride and the geranyl chloride should be close together. From this it follows that the geranyl chloride obtained from isoprene hydrochloride can react with isoprene to form polyterpene chlorides. The accumulation of geranyl chloride in the mixture in the initial stages of reaction depends on a high concentration of starting isoprene hydrochloride and a small concentration of geranyl chloride, so that the rate of formation of geranyl chloride is much higher than the rate of its destruction. As the starting hydrochloride is used up and the geranyl chloride is formed, the rate of the primary reaction gradually lessens, and that of the second rises. This leads at a certain moment to a kinetic equilibrium between both reactions and the increase of geranyl chloride stops. When the starting halogen is further used up, the second reaction begins to predominate, the content of geranyl chloride in the mixture decreases and in time disappears entirely. Along with this, the content of isomeric monoterpene chlorides in the mixture constantly increases. This is evidently due to their relatively lower reactivity compared to that of the starting halogen compounds, so that they accumulate in the reaction mixture.

EXPERIMENTAL

Method of conducting the experiments. A round bottomed flask was fitted with a stirrer, reflux condenser, thermometer, and dropping funnel. A glass tube was led to the bottom of the flask and was connected to a small cylindrical vessel with an aerometer. In the flask was placed an equimolecular mixture of isoprene with its hydrochloride and methylene chloride. It was cooled externally with ice and salt and a 2% solution of anhydrous tin chloride in methylene chloride was added with stirring through the dropping funnel until definite signs of reaction appeared (rise of temperature in the mixture). Then the mixture was sucked over into the cylinder with the aerometer with a plastic bulb, and its density was determined at the beginning of the reaction and the mixture was at once forced back into the reaction vessel with the same bulb. Density determinations were carried out every 2 minutes. When the desired density of the reaction mixture had been reached, reaction was stopped by adding a water solution of sodium chloride to the mixture. The product was repeatedly washed with water and dried over potash. The solvent and the unreacted starting reagents were distilled off on the water bath, at first at atmospheric pressure, then in a vacuum. The terpene chloride (C_{10}) fraction was distilled from the remaining telomerization product on the water bath at 2-1 mm pressure (b.p. 60-90° at 2 mm).

The geranyl chloride content in a mixture was found in the following way: the total amount of saponifiable chloride in the mixture of chlorides was determined by boiling a sample with an alcohol-water solution of $Pb(NO_3)_2$ for 2 hours. The corresponding amount of acid was then evolved according to the equation.

$$2RCl + Pb(NO_3)_2 + 2H_2O \rightarrow 2ROH + PbCl_2 + 2HNO_3,$$

and after addition of excess aqueous solution of NaCl this was titrated with alkali in the presence of bromphenol blue.

Another sample of chlorides (25 g) was transferred to a 200 ml flask fitted with a reflux condenser and to it was added 20 g of urotropine and 100 ml of dried methylene chloride. The mixture was heated for 3 hours on the water bath. The resulting complex compound of geranyl chloride with urotropine was removed by water and the remaining solution of terpene chlorides in methylene chlorides was washed repeatedly, weighed, and its content of saponifiable chloride was determined by the method described above.*

The geranyl chloride content of the mixture was found by the difference in amount of saponifiable chloride in the starting mixture and in the remaining chlorides.

The results of the experiments are given in tha Table.

Effect of Intensity of Reaction on Composition of the Telomerization Products

Experiment No.	Composition of reaction mixture (in g)			Reaction temperature	Duration of reaction (in min)	Change in mixt. density d_4^{20}		Telomerization product		Amt. of isoprene (bound and free) which reacts (in %)	Terpene chloride fraction		
	Hydrochloride & isoprene mixt. (20.5% Cl)	solvent	catalyst			at beginning of reaction	at end of reaction	yield (in g)	chlorine content (in %)		yield of telomer (%)	chlorine content (%)	geranyl chloride content (%)
1	1430	1580	0.6	18°	19	1.015	1.030	157	17.2	11.5	64.0	20.2	63.5
2	1420	1600	0.6	19	18	1.016	1.036	272	16.4	20.2	51.5	20.0	60.6
3	1413	1775	0.6	18	31	1.043	1.069	379	15.7	28.5	45.9	20.1	57.5
4	500	770	0.4	15	18	1.072	1.108	212	14.9	46.6	37.2	19.6	49.8
5	500	640	0.45	20	17	1.048	1.090	247	14.4	53.2	33.0	19.4	46.3
6	300	380	0.3	19	68	1.046	1.148	570	16.5	88.0	6.2	16.0	16.2

SUMMARY

1. We have studied the effect of intensity of reaction on composition of the telomerization product of isoprene and its hydrochloride in the presence of anhydrous tin chloride.

2. We have shown that the intensity of reaction is a decisive factor which determines the composition of the reaction products: in the initial stages of reaction, geranyl chloride predominates in the reaction product, and in the final stages polyterpene chlorides and isomeric monoterpene chlorides (terpenyl chloride) are the main products.

3. We have confirmed the idea which was suggested earlier that it is necessary to interrupt their reaction in the early stages in order to obtain a maximum yield of terpene chlorides in the telomerization of isoprene with halogen compounds.

4. The results of this study have been considered from the viewpoint of the ideas expressed earlier of the two kinetic steps in the process of telomerization in the presence of ionic catalysts.

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THE CHLORINATION OF ETHYLENE GLYCOL

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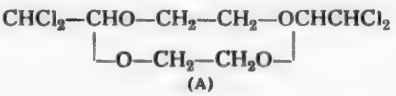
The chlorination of monoatomic alcohols has been studied in sufficient detail. However, there is very little data in the literature on the reaction of chlorine with diatomic alcohols, especially with ethylene glycol. Even in 1863, Mitscherlich [1] noticed an intense reaction of chlorine with ethylene glycol and isolated a fraction with boiled at 108-200° and contained chlorine and a fraction which boiled above 200° and did not contain chlorine. However, the composition of these fractions remained unknown. Later Donciu [2] chlorinated ethylene glycol at 140-180° and obtained a mixture from which he isolated and identified ethylene chlorohydrin, 2-(β-chloroethoxy)-3-hydroxy-1,4-dioxane, and some carbonyl compounds. He also suggested the possibility of forming polyethylene glycol. There are no later studies in the literature.

It appeared interesting to us to investigate this reaction in more detail. Chlorination of ethylene glycol at room temperature without illumination goes very slowly, and so we turned to initiation by ultraviolet light. We then found a very energetic absorption of chlorine by ethylene glycol with evolution of heat so that the temperature of the mixture reached a maximum of 127°. The original weight was increased by 70-80%. As a result we obtained a mixture of products consisting of 27% β-chloroethyl dichloroacetate, 15% of the previously undescribed cyclic acetal A, 12% water, 11% dichloroacetaldehyde, 11% ethylene chlorohydrin, 6% 2-dichloromethyl-1,3-dioxolane, and small admixtures of oxalic and dichloroacetic acids.



(A)

The structure of the above mentioned acetal was confirmed by splitting it with concentrated hydrochloric acid, as a result of which we obtained dichloroacetaldehyde and ethylene chlorohydrin. The chlorination of ethylene glycol, initiated by the addition of 0.2% $SbCl_3$ gives about the same composition of the mixture as does chlorination in ultraviolet. However, in this case the above mentioned high boiling acetal of ethylene glycol and $CHCl_2CHO$ are absent from the reaction product.

The separation of the different products from the mixture was made difficult by the presence of a large amount of HCl which caused considerable tarring of the products in distillation. Therefore, before separation of the mixture it was carefully freed from HCl.

Since the chief reaction product of chlorination of ethylene glycol in ultraviolet is β-chloroethyl dichloroacetate, it became interesting to study the action of chlorine on this ester in order to explain the nature of the high boiling products. We ran experiments on the chlorination of this ester in the ultraviolet which showed that we obtained a yield of 62% of α,β,β',β'-tetrachloroethyl trichloroacetate.

Thus, in the reaction of chlorine with ethylene glycol under ultraviolet illumination or in the presence of a catalyst the processes of oxidation and chlorination occur simultaneously, accompanied by secondary reactions: esterification and acetal formation. We must assume that here, as in the case of monoatomic alcohols, the first action of chlorine on ethylene glycol is the oxidation of one or two of the hydroxyls with formation of the corresponding glyoxal and glycolic aldehyde, which, however, could not be isolated, evidently because of its rapid transformation to oxalic acid.

$$CH_2OH-CH_2OH + Cl_2 \rightarrow \begin{matrix} CHO-CHO \\ CH_2OH-CHO \end{matrix} + HCl \xrightarrow{(O)} COOH-COOH$$

The hydrogen chloride which was then evolved formed ethylene chlorohydrin with ethylene glycol [3] which then reacted with chlorine according to the equation

$$\underset{(I)}{CH_2Cl-CH_2OH} + Cl_2 \rightarrow \underset{(II)}{CH_2Cl-CHO} + HCl$$

Chloroacetaldehyde could also be formed according to the equation

$$CH_2OH-CHO + HCl \rightarrow CH_2Cl-CHO + H_2O$$

Chlorination of chloroacetaldehyde took place simultaneously to dichloroacetaldehyde which in the presence of water was oxidized to dichloroacetic acid. Dichloroacetic acid and ethylene chlorohydrin formed an ester which could be further chlorinated. In the presence of mineral acids the carbonyl compounds easily formed cyclic acetals and ketals with vicinal glycols [4].

$$CHCl_2CHO + CH_2OH-CH_2OH \rightarrow \begin{cases} \underset{(IV)}{CHCl_2-CHO-CH_2CH_2O} \\ CHCl_2-CHO-CH_2CH_2OCH-CHCl_2 \\ \qquad\qquad\qquad\quad | \\ \qquad\qquad\qquad\quad -O-CH_2-CH_2-O \\ \qquad\qquad\qquad\quad \underset{(VI)}{} \end{cases}$$

EXPERIMENTAL

Chlorination of ethylene glycol. In a quartz reaction vessel fitted with a thermometer and reflux condenser was placed 346 g of ethylene glycol with b.p. 187.5-188.5° and $n^{20}D$ 1.4312. Dry chlorine was introduced through a bubbler of porous glass plate. The reaction vessel had a quartz mercury source PRK-2 placed at a distance of 9 cm. During the chlorination the temperature rose to 127°. The reaction was considered to be complete when increase in weight stopped. Chlorination lasted 14-16 hours. When the liquid stood, it separated and precipitated colorless crystals of oxalic acid in the amount of 15 g with m.p. 101.5° (from ether).

Found %: C 19.38; H 4.50. M 130.7, 129.6 (according to Rast). $C_2H_2O_4 \cdot 2H_2O$. Calculated %: C 19.05; H 4.76. M 126.

A mixed melting point with oxalic acid dihydrate showed no depression. In the filtrate we determined by the Fischer reagent 77 g of water, the greater part of which could be removed over ignited Na_2SO_4. To remove HCl, dry nitrogen was passed through the product. The substances carried off by the nitrogen were caught in a trap filled with acetone and solid carbon dioxide. For more complete uptake of HCl the product was kept for a long time over calcium carbonate. As a result we obtained 395.6 g of liquid. The data on distillation are given in the Table.

Results of the Distillation of the Product from the Chlorination of Ethylene Glycol in Ultraviolet Light

Fraction	B. p. (pressure in mm)	Wt. (in g)	n_D^{20}
A	97—107° (760)	130.0	1.4425
B	55— 74 (4)	23.0	1.4660
C	74— 78 (4)	101.0	1.4711
D	78—150 (4)	28.0	1.4711
E	150—170 (3)	55.0	1.4959
Residue		31.0	
		368.0	

Fraction A is mixed with water; the remaining fractions are unmixed.

Fraction A contained ethylene chlorohydrin, dichloroacetaldehyde, and water. Since the azeotropic mixture ethylene chlorohydrin—water has a boiling point lying close to those of dichloroacetaldehyde hydrate and water, they could not be separated by distillation, and so their separation was carried out from the mixture. The amount of water, determined by the Fischer method, was 43 g. Hydrogen chloride was removed from 30 g of fraction A by NaOH to give 3.5 g of ethylene oxide. When we formed a derivative of(II) with phenylhydrazine,

instead of the expected phenylhydrazone [5] there was formed an osazone hydrochloride (III) analogous to the reaction of (II) with hydroxylamine hydrochloride [6]. From 10 g of fraction A we obtained 3.5 g of (III) with a m.p. 233-234° (from alcohol).

A mixed melting point with the osazone hydrochloride obtained from dichloroacetaldehyde synthesized from trichloroacetic acid [7] showed no depression.

Found %: C 53.38; H 5.61; Cl 23.08; N 18.20. $C_{14}H_{16}N_4Cl_2$. Calculated %: C 54.00; H 5.15; Cl 22.82; N 18.00.

Preliminary study of fraction B showed that it approached the composition of an acetal. Since the acetal was stable to alkali, its separation was made easier by treating the liquid with alkali to free it from esters of ethylene chlorohydrin which were present. 23 g of fraction B, 10 g NaOH and 50 ml of water were boiled 2 hours under reflux, then extracted with ether. As a result we obtained 10 g of 2-dichloromethyl-1,3-dioxolane (IV). After repeated distillations, substance (IV) was isolated.

B. p. 69-72° (9 mm), $n^{20}D$ 1.4754, d^{20}_4 1.4147, MR_D 31.46; calc. 31.49.
According to [8]: b.p. 185-188°.
Found %: C 30.46; H 3.06; Cl 45.47. M 158.4 (cryoscopic). $C_4H_6O_2Cl_2$. Calculated %: C 30.57; H 3.82; Cl 45.22. M 157.

2 g of (IV) and 4.6 g of concentrated hydrochloric acid were boiled under reflux until the layers disappeared, and the mixture was then put over calcium carbonate to a neutral reaction. From it we obtained 2.9 g of (III) and we detected (I) qualitatively (by the formation of ethylene oxide when hydrogen chloride was removed).

Fraction C consisted of β-chloroethyl dichloroacetate (V) with a small admixture of the free acid. From 10.8 g of this fraction we obtained 1.5 g of the aniline salt of dichloroacetic acid with m.p. 123-124° (from benzene with alcohol).

Found %: C 42.50; H 3.69; Cl 31.40; N 5.86. Equiv. 222, 223. $C_8H_9O_2NCl_2$. Calculated %: C 43.24; H 4.05; Cl 31.98; N 6.30. Equiv. 222.

A mixed m.p. with the aniline salt of dichloroacetic acid synthesized from chloral [9] showed no depression. Repeated distillation of the remaining 90 g of fraction C gave 83 g (V).

B.p. 79-82° (7 mm), $n^{20}D$ 1.4722.
According to [10]: b.p. 209-212°.
Found %: C 24.68; H 2.01; Cl 54.78. M 196.4, 195.2 (cryoscopic). $C_4H_5O_2Cl_3$. Calculated %: C 25.06; H 2.61; Cl 55.61. M 191.5.

Saponification of 72 g of (V) by NaOH solution gave 6.8 g of ethylene oxide and 26.8 g of dichloroacetic acid.

Fraction D was not identified; it consisted of a mixture of esters formed by deeper chlorination, with very similar boiling points, and so it was impossible to separate individual substances by distillation.

Fraction E treated like fraction B gave 37 g of acetal (VI). After two distillations we obtained substance (VI).

B.p. 166-170° (3 mm), $n^{20}D$ 1.4910, d^{20}_4 1.4552, MR_D 62.29; calc. 62.98.
Found %: C 30.99; H 3.42; Cl 45.12. M 313 (cryoscopic) $C_8H_{12}O_4Cl_4$. Calculated %: C 30.57; H 3.82; Cl 45.22. M 314.

Splitting with concentrated hydrochloric acid, as with (IV), gave, from 1.6 g of (VI), 3.1 g of (III), and (I) was detected qualitatively.

Chlorination of β-chloroethyl dichloroacetate. 48.5 g of β-chloroethyl dichloroacetate (V) (b.p. 75-78° at 3 mm, $n^{20}D$ 1.4707) was isolated from the chlorination product of ethylene glycol and purified by distillation three times; it was chlorinated under conditions analogous to those for chlorination of ethylene glycol. The temperature did not rise above 34°. After 45 hours, increase in weight stopped. It was freed from HCl as ethylene glycol had been. As a result we obtained 78.5 g of chlorination product. By twice redistilling we isolated 30 g of α,β,β',β"-tetrachloroethyl trichloroacetate (VII).

B.p. 90-92° (2 mm), $n^{20}D$ 1.4991, d^{20}_4 1.6966, MR_D 56.73; calc. 56.39.
Found %: C 14.61; H 0.55; Cl 74.97. M 327. (cryoscopic). $C_4HO_2Cl_7$. Calculated %: C 14.56; H 0.30; Cl 75.41. M 329.5.

From 8.5 g of (VII) by ammonolysis we obtained 2.3 g of a substance with m.p. 138° (sublimation) which gave no depression by mixed melting point with trichloroacetamide.

Chlorination of ethylene glycol in the presence of $SbCl_3$. When ethylene glycol was chlorinated with the addition of 0.2% $SbCl_3$ there was energetic reaction with evolution of heat, and the temperature reached a maximum of 110°. The original weight increased by 50-60%. The chlorination product was treated like the chlorination product in ultraviolet light. Altogether, the following substances were found HCl, H_2O, $(COOH)_2 \cdot 2H_2O$, $CHCl_2CHO$, $CHCl_2COOH$, $CHCl_2CHO-CH_2-CH_2O$ and $CHCl_2-COOCH_2CH_2Cl$.

SUMMARY

1. We have studied the chlorination of ethylene glycol initiated by ultraviolet light. We have isolated and identified the following products: β-chloroethyl dichloroacetate (27%), an acetal of the structure $CHCl_2-CHO-CH_2-CH_2-OCHCHCl_2$ (15%), water (12%), dichloroacetaldehyde (11%), ethylenechlorohydrin

$$\left|-OCH_2-CH_2-O-\right|$$

(11%), 2-dichloromethyl-1,3-dioxolane (6%), and admixtures of oxalic and dichloroacetic acids. We have found that when ethylene glycol is chlorinated in the presence of $SbCl_3$ the same products are formed, except for the second.

2. We have shown that when β-chloroethyl dichloroacetate is chlorinated in ultraviolet light, α,β,β',β"-tetrachloroethyl trichloroacetate is obtained in 62% yield.

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STUDIES IN THE FIELD OF GLYCOL ETHERS AND THEIR DERIVATIVES

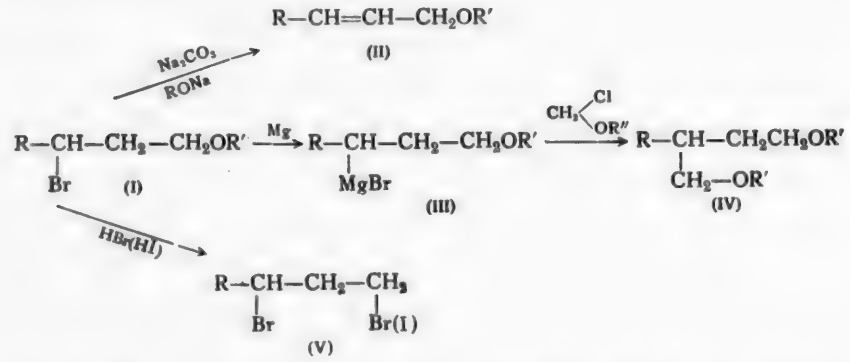
XXXIII. SOME CHEMICAL TRANSFORMATIONS OF γ-BROMOETHERS OF THE ALIPHATIC SERIES

Shamkhal Mamedov and B. K. Zeinalov

It was shown earlier that γ-bromoethers are easily obtained by alkylation of α-bromoethers by ethylene hydrocarbons [1]. It is interesting to investigate some chemical transformations of the γ-bromoethers, which, according to the literature, are almost unknown [2, 3].

Experiments on the hydrolysis of γ-bromoethers (I) carried out in the presence of Na_2CO_3 and $CaCO_3$ (10-12 hours) showed that HBr was then split out with the formation of ethers of allyl alcohol homologs (II). In all cases, instead of the expected product, the partial ethers of the β-glycols, we obtained unsaturated ethers. When the γ-bromoethers were heated with a solution of alcoholic alkali, the splitting out of HBr ended much sooner (2-3 hours). When sodium alcoholate acted on these bromoethers (I), instead of the expected etherification reaction, there occurred splitting out of HBr with formation of the allyl ethers (II). The order of splitting out of HBr agreed with the Markovnikov rule, which was shown by establishing the structures of the allyl ethers by oxidation [1].

The negative results of the hydrolysis and etherification reactions are evidently due to some mobility of the hydrogen in the β-position with respect to the oxygen bridge in the γ-haloethers (I); on the other hand, the presence of bromine on the secondary carbon atom apparently makes the splitting out of HBr easier. γ-Bromoethers (I) like γ-chloroethers [1] easily give magnesium organic compounds (III) which can react with α-chloroethers to form 1,4-glycol ethers (IV). In this way a new possibility has been discovered for the synthesis of glycol ethers with different alkoxy groups in the 1,4-positions (IV).



γ-Bromoethers (I), like γ-chloroethers [1], under the action of HBr or HI form the corresponding 1,3-dihalo derivatives (V). In this way we synthesized and studied 6 new examples of 1,3-dihalo derivatives of saturated hydrocarbons whose constants are given in the Table.

Constants of 1,3-Dihalo Derivatives

No.	Structural formula R–CH(X)–CH₂–CH₂(Y): R	X	Y	Name of dihalogen compound	Boiling point (pressure in mm)	d_{20}^{20}	n_D^{20}	MR_D found	MR_D calc.	M found	M calc.	Halogen content (in %) found	Halogen content (in %) calc.	Yield (%)
1	CH_3	Br	I	1-Iodo-3-bromobutane C_4H_8BrI	66—67° (15)	1.9600	1.5340	41.71	41.23	269.7	263.0	77.81	78.54	76.4
2	CH_3	Cl	Br	1-Bromo-3-chlorobutane C_4H_8ClBr	45—47 (12)	1.4503	1.4736	33.21	33.30	172.9	171.5	67.17	67.34	75.8
3	CH_3	Cl	I	1-Iodo-3-chlorobutane C_4H_8ClI	52—54 (5)	1.7500	1.5230	38.14	38.33	220.7	218.5	74.61	74.37	68.7
4	C_2H_5	Br	I	1-Iodo-3-bromopentane $C_5H_{10}BrI$	84—86 (18)	1.8332	1.5290	46.63	45.86	281.6	277.0	75.28	74.73	79.3
5	C_2H_5	Cl	Br	1-Bromo-3-chloropentane $C_5H_{10}ClBr$	53—55 (10)	1.3900	1.4734	37.46	37.92	188.3	185.5	61.98	62.26	81.1
6	C_2H_5	Cl	I	1-Iodo-3-chloropentane $C_5H_{10}ClI$	55—57 (5)	1.6600	1.5200	42.58	42.95	234.2	232.5	70.17	69.89	81.9

These chemical transformations indicate the possibility of the synthesis of a series of organic compounds whose starting substances can be the products of alkylation of γ-bromoethers by ethylene hydrocarbons, especially 1,3-dihalo derivatives of hydrocarbons which contain not only the same, but also different halogens in the molecule.

EXPERIMENTAL

Action of an aqueous soda solution on butyl bromobutyl ether (I, R = CH_3, R' = n-C_4H_9). To a solution of 15 g of Na_2CO_3 in 150 ml of water was added 20.9 g of the bromoether (I) and the resulting mixture was heated for 15 hours. The reaction product was extracted with ether. After drying and distilling off the solvent, a vacuum distillation gave 6 g (45%) of butyl γ-methylallyl ether (II, R = CH_3, R' = n-C_4H_9).

B.p. 154-156°, d_{20}^{20} 0.8100, $n^{20}D$ 1.4150, MR_D 39.57. $C_8H_{16}F$. Calculated 40.32. Found M 125. Calculated 128.

The position of the double bond in the allyl ethers obtained from γ-haloethers was shown by oxidation [1].

Under analogous conditions Na_2CO_3 was replaced by $CaCO_3$ and in this case the same splitting out of HBr occurred.

Thus, for example, by heating a mixture of 16.7 g of methyl γ-bromobutyl ether (I, R = R' = CH_3) and 15 g of chemically pure $CaCO_3$ with 150 ml of water for 14 hours we obtained 3.5 g (40%) of methyl γ-methylallyl ether (II, R = R' = CH_3).

B.p. 78-81°, d_{20}^{20} 0.7972, $n^{20}D$ 1.4010, MR_D 26.21. $C_5H_{10}F$. Calculated 26.46. Literature data [4]: b.p. 79°, d^0 0.8035.

Action of alcoholic alkali on methyl γ-bromoamyl ether (I, R = C_2H_5, R' = CH_3). A mixture of 18 g of bromoether, 5.6 g of KOH and 10 ml of 95% ethyl alcohol was heated on the water bath for 3 hours. After the usual treatment we obtained 6.5 g (56%) of methyl γ-ethylallyl ether (II, R = C_2H_5, R' = CH_3).

B.p. 103-106°, d_{20}^{20} 0.7910, $n^{20}D$ 1.4030, MR_D 30.35. $C_6H_{12}OF$. Calculated 31.08. Found M 102.1. Calculated 100.

Action of sodium ethylate on butyl γ-bromoamyl ether (I, R = C_2H_5, R' = n-C_4H_9). 2.3 g of metallic sodium was dissolved in 8 g of anhydrous alcohol and then 22.3 g of γ-bromoether was added to the mixture and the reaction flask was heated for

4 hours on the water bath; then water was added to the flask and the product was extracted by ether. After drying and distilling off the solvent, vacuum distillation gave 8 g (55%) of butyl γ-ethylallyl ether [1] (II, R = C_2H_5, R' = = n-C_4H_9).

B.p. 169-172°, d^{20}_{20} 0.8090, $n^{20}D$ 1.4200, MR_D 44.42. $C_8H_{18}OF$. Calculated 44.93.

Action of α-chloroethers on the magnesium organic compounds prepared from γ-bromoether (I). From 2.4 g of magnesium and 18.2 g of butyl α-bromobutyl ether (I, R = C_2H_5, R' = n-C_4H_9) we prepared the magnesium organic compound (III) by the method described in previous work [1]. Then the resulting Grignard reagent we added 12.3 g of α-chloromethyl ether. The reaction flask was heated on the water bath with stirring for 1 hour. After the usual treatment we obtained 6 g of 2-ethyl-1-methoxy-4-butoxybutane (IV, R = C_2H_5, R' = n-C_4H_9, R" = CH_3).

B.p. 205-208°, d^{20}_{20} 0.8540, $n^{20}D$ 1.4200, MR_D 55.71. $C_{11}H_{24}O_2$. Calculated 56.28. Found M 183. Calculated 188.

The structure of the resulting ether was established by the action of HBr on it: 5 g of the ether was saturated with gaseous HBr at −10° and heated in a sealed tube at 100° for 12 hours. Vacuum distillation gave 5 g of 2-ethyl-1,4-dibromobutane.

B.p. 84-86° (12 mm), d^{20}_{20} 1.6510, $n^{20}D$ 1.5180, MR_D 44.78. $C_6H_{12}Br_2$. Calculated 45.43.

Action of HBr on methyl γ-bromoamyl ether (I, R = C_2H_5, R' = CH_3). The experiment was carried out as previously described [1]. From 18 g of the γ-bromoether we obtained 20 g of the 1,3-dibromopentane (V, R = = C_2H_5).

B.p. 63-65° (10 mm), d^{20}_{20} 1.6683, $n^{20}D$ 1.5066, MR_D 41.00. $C_6H_{10}Br_2$. Calculated 40.82.
Literature data [5]: b.p. 190-195° (750 mm), d^{20}_4 1.6720, $n^{20}D$ 1.5048.

Action of HI on methyl γ-bromoamyl ether (I, R = C_2H_5, R' = CH_3). 18 g of the bromoether was saturated with HI at 0°. The cylinder was closed with a ground glass stopper and kept at room temperature for 36 hours. The reaction mixture was poured into cold water. The lower layer was washed with 2% sodium hydroxide and with water. After drying and vacuum distillation we obtained 18 g of 1-iodo-3-bromopentane, whose constants are given in the Table (substance 4).

In an analogous way, by the action of HBr or HI on γ-bromo- and γ-chloroethers we obtained the other 5 new mixed 1,3-dihalogen derivatives of saturated hydrocarbons whose constants are given in the Table.

SUMMARY

1. We have shown that when γ-bromoethers are heated with solutions of Na_2CO_3, $CaCO_3$, and sodium alcoholate, splitting out of HBr occurs, with formation of allyl ethers.

2. Magnesium organic compounds prepared from γ-bromoethers react smoothly with α-chloroethers with formation of the ethers of 1,4-glycols.

3. We have studied the action of HBr and HI on γ-bromo- and γ-chloroethers. We have shown that this forms 1,3-dihalogen derivatives of saturated hydrocarbons in yields up to 80%.

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STUDIES IN THE FIELD OF GLYCOL ETHERS AND THEIR DERIVATIVES.

XXXIV. CHEMICAL TRANSFORMATIONS OF γ-CHLOROETHERS

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The chemical transformations of γ-chloroethers have been very little studied [1-3]. It was shown earlier [4] that ethers of homologs of allyl alcohol (II), for the synthesis of which the existing methods are not satisfactory [5-8], can be obtained by splitting out HCl from γ-chloroethers (60%). It becomes interesting to make a more detailed study of the properties of the ethers of allyl alcohol homologs (II) which, according to the literature, have hardly been studied.

When hydrogen halides act on allyl ethers (II) the double bond of the ether remains untouched and the oxygen bridge is easily broken with the formation of unsaturated (III) and saturated (IV) halogen derivatives of hydrocarbons [9, 10]. However, as our experiments showed, HCl and HBr in the presence of a catalyst ($ZnCl_2$) combine smoothly at the double bond of the allyl ethers even in the cold (at 0°). The reaction product is the corresponding γ-haloether, which we have isolated and identified. Hence, addition of the hydrogen halide occurs in such a way that the hydrogen goes to the carbon nearest the oxygen bridge (according to the Markovnikov rule).

The reaction with the catalyst can be presented by the following scheme, in accord with the work of Kondakov [11].

$$R{-}CH{=}CH{-}CH_2OR' \xrightarrow{ZnCl_2} \underset{(II)}{R{-}CH(Cl){-}CH(ZnCl){-}CH_2OR'} \xrightarrow{HCl} \underset{(III)}{} \longrightarrow \underset{(I)}{R{-}CH(Cl){-}CH_2{-}CH_2OR'} + ZnCl_2$$

When hydrogen bromide acts on allyl ethers in the presence of $ZnBr_2$, the chief product is the γ-bromoether (V). However, in the case of excess HBr, deeper reaction occurs and there is also formation of a certain amount of 1,3-dibromo derivative of the hydrocarbon.

$$\underset{(I)}{R{-}CH(Cl){-}CH_2{-}CH_2OR'} \underset{ZnCl_2 + HCl}{\overset{NaOH + alcohol}{\rightleftharpoons}} \underset{(II)}{R{-}CH{=}CH{-}CH_2OR'} \xrightarrow{HBr} \underset{(V)}{R{-}CH(Br){-}CH_2{-}CH_2(Br)}$$

$$\underset{(II)}{R{-}CH{=}CH{-}CH_2OR'} \xrightarrow{Br_2} \underset{(VI)}{R{-}CH(Br){-}CH(Br){-}CH_2OR'}$$

$$\underset{(I)}{R{-}CH(Cl){-}CH_2{-}CH_2OR'} \xrightarrow{Mg} \underset{(VII)}{R{-}CH(MgCl){-}CH_2{-}CH_2OR'} \xrightarrow{[O]} \underset{(IX)}{R{-}CH(OH){-}CH_2{-}CH_2OR'}$$

$$\underset{(VII)}{R{-}CH(MgCl){-}CH_2{-}CH_2OR'} \xrightarrow{CO_2} \underset{(VIII)}{R{-}CH(COOH){-}CH_2{-}CH_2OR'}$$

When bromine acts on allyl ethers (II) in the cold (−15°) it gives β,γ-dibromoethers (VI) in good yield (75%). This method opens many possibilities for obtaining different β,γ-dibromo derivatives of ethers which are suitable for organic syntheses.

Magnesium organic compounds (VII) prepared from γ-chloroethers [4] are easily oxidized by pure oxygen and oxygen of the air. In the latter case oxidation proceeds more moderately and as a result magnesium haloglycolates are obtained, which with water give monoethers of β-glycols (IX) with yields of 10-15%. These Grignard reagents (VII) rapidly absorb carbon dioxide gas with the formation of magnesium salts of hydroxyacid ethers which by further treatment with dilute acids form ethers of γ-hydroxyacids (VIII).

EXPERIMENTAL

The synthesis of allyl ethers was carried out under the conditions described earlier [4]. The constants for the allyl ethers which were synthesized are given in Table 1.

TABLE 1

Allyl Ethers

No.	Struct. formula of ethers R–CH=CH–CH₂OR′		Name of ether	Boiling point	d_{20}^{20}	n_D^{20}	MR_D		M		Yield (in %)
	R	R′					found	calc.	found	calc.	
1*	C_2H_5	C_2H_5	Ethyl γ-ethylallyl ether	123—127°	0.7981	1.4093	35.34	35.70	117.2, 112.4	114.0	41.25
2**	C_2H_5	CH_3	Methyl γ-ethylallyl ether	104—108	0.7899	1.4023	30.85	31.08	—	—	36.4
3**	C_2H_5	C_4H_9-n.	Butyl γ-ethylallyl ether	170—174	0.8083	1.4198	44.44	44.93	—	—	62.35

*First time synthesized. The structure of the allyl ether obtained from the γ-chloroether was shown by oxidation [4].

**Agrees with the results for the allyl ethers obtained from the corresponding γ-bromoethers (paper XXXIII).

Action of HCl on butyl γ-methylallyl ether (II, R=CH_3, R′=n-C_4H_9) in the presence of $ZnCl_2$. To 4 g of allyl ether was added 0.5 g of $ZnCl_2$ and after the mixture was cooled to 0°, dry HCl was passed through it for 6 hours. After washing, drying, and distilling repeatedly we obtained 0.8 g of butyl γ-chlorobutyl ether (I, R=CH_3, R′ = n-C_4H_9) [4].

B.p. 67-68° (19 mm), d_{20}^{20} 0.9020, $n^{20}D$ 1.4160, MR_D 45.47. $C_9H_{19}OCl$. Calculated 45.65.

Action of HBr on butyl γ-methylallyl ether (II, R = CH_3, R′ = n-C_4H_9). To 3 g of allyl ether was added 0.3 g of anhydrous $ZnBr_2$. The mixture was cooled with ice water, HBr was passed through it for 3 hours, and the washed and dried reaction product was vacuum distilled at 20 mm. We obtained the fractions: 1) 52-69°, 0.5 g; 2) 69-72°, 1.2 g; 3) 72-104°, 0.7 g; 4) 105-109°, 1.5 g; residue 0.8 g.

TABLE 2

β,γ-Dibromoethers

No.	Structural formula of ethers R–CH(Br)–CH(Br)–CH₂OR′ R	R′	Name of ether	Boiling point (pressure in mm)	d_{20}^{20}	n_D^{20}	MR_D found	MR_D calc.	M found	M calc.	Bromine content (in %) found	Bromine content (in %) calc.	Yield (in %)
1	CH_3	C_4H_9-n	Butyl β,γ-dibromo-butyl ether	122° (16)	1.4627	1.4880	56.74	56.31	283.5	288	55.75	55.56	77
2	C_2H_5	C_4H_9-n	Butyl β,γ-dibromo-amyl ether	127—128 (16)	1.4413	1.4910	60.70	60.93	297.0	302	52.58	52.98	67
3	C_2H_5	C_2H_5	Ethyl β,γ-dibromo-amyl ether	120 (20)	1.4982	1.4819	52.14	51.70	272.8	274	58.42	58.39	75

TABLE 3

Partial Ethers of 1,3-Diols

No.	Structural formula of ethers R–CH(OH)–CH₂–CH₂OR′ R	R′	Name of ether	Boiling point (pressure in mm)	d_4^{20}	n_D^{20}	MR_D found	MR_D calc.	M found	M calc.	% C found	% C calc.	% H found	% H calc.	% (OH) found	% (OH) calc.	Yield (in %)
1	CH_3	C_2H_5	1-Ethoxy-3-butanol	175—178°	0.9051	1.4246	33.31	33.08	121.9	118	61.11	61.01	11.95	11.88	15.04	14.41	15.7
2	C_2H_5	CH_3	1-Methoxy-3-pentanol	77—82 (23)	0.9163	1.4262	33.01	33.08	120.4	118	61.41	61.01	11.81	11.88	14.31	14.41	12.3
3	C_2H_5	C_2H_5	1-Ethoxy-3-pentanol	82—85 (20)	0.8971	1.4223	37.41	37.69	129.5	132	63.51	63.63	12.15	12.12	13.75	12.88	11.4

Fraction 2 was 1,3-dibromobutane:

d^{20}_{20} 1.7756, $n^{20}D$ 1.5092, MR_D 36.36. CH_8Br_2. Calculated 36.20 [12].

Fraction 4 was butyl γ-bromobutyl ether (V, R = CH_3, R' = n-C_4H_9):

d^{20}_{20} 1.1395, $n^{20}D$ 1.4468, MR_D 49.01. $C_8H_{17}OBr$. Calculated 48.55 [4].

Synthesis of β,γ-dibromobutyl ether (VI, R = CH_3, R' = n-C_4H_9). 2 g of butyl γ-methylallyl ether (II, R = CH_3, R' = n-C_4H_9) was placed in a test tube and the calculated amount of bromine was added to it dropwise with cooling (−15°) and shaking. After it was washed and dried, the reaction product was vacuum distilled. We obtained 3.5 g (77%) of β,γ-dibromoether (VI, R = CH_3, R' = n-C_4H_9) (Table 2, substance 1). In an analogous manner we obtained two more new β,γ-dibromoethers whose constants are given in Table 2.

Oxidation of magnesium organic compounds (VII, R = CH_3, R' = C_2H_5). From 1.8 g of magnesium and 11 g of ethyl γ-chlorobutyl ether (I, R = CH_3, R' = C_2H_5) was prepared the magnesium organic compound (VII, R = CH_3, R' = C_2H_5) through which a stream of dry air was passed (14 liters) at 0° for 2.5 hours. The oxidation product was decomposed with dilute hydrochloric acid. After washing, drying, and distilling off the solvent we submitted the product to fractional distillation. We obtained 1.5 g (15.7%) of the monoethyl ether of 1,3-butanediol (Table 3, substance 1). The experiment was repeated with pure oxygen. The yield of monoether was 13.6%.

In an analogous manner we obtained two more monoethers whose constants are given in Table 3.

Action of carbon dioxide on the magnesium organic compound (VII, R = CH_3, R' = n-C_4H_9). From 2.4 g of magnesium and 16.5 g of butyl γ-chlorobutyl ether (I, R = CH_3, R' = n-C_4H_9) we prepared the magnesium organic compound in the usual way, and passed through it a stream of dry carbon dioxide gas with cooling (5°). After the usual treatment we obtained 4 g of a liquid with b.p. 141-144° (5 mm), d^{20}_{20} 0.9328, $n^{20}D$ 1.4308. The product had acid properties and by analysis of its silver salt (needles from alcohol) was γ-butoxy-α-methyl butyric acid (VI, R = CH_3, R' = n-C_4H_9).

Found %: Ag 38.32. $C_9H_{17}O_3Ag$. Calculated %: Ag 38.39.

SUMMARY

1. We have given a method for the synthesis of β,γ-dibromo derivatives of ethers.

2. We have shown that by the action of HBr and HCl on allyl ethers in the presence of $ZnCl_2$ or $ZnBr_2$ there is an addition reaction with formation of γ-haloethers.

3. We have established that by the oxidation of magnesium organic compounds prepared from γ-chloroethers, monoethers of β-glycols are formed as magnesium halogen alcoholates.

4. We have established that by the action of carbon dioxide on the magnesium organic compounds prepared from γ-chloroethers, ethers of γ-hydroxy acids are formed.

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N-DI(CHLOROETHYL)AMINES OF THE ALICYCLIC SERIES. I.

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The search for anti-cancer substances among the nitrogen analogs of yperite [N-di(chloroalkyl)amines] has continued until now. The basic purpose of work in this direction is to find substances with the greatest effectiveness and the lowest toxicity. Investigators have studied aliphatic, aromatic, fatty-aromatic, heterocyclic, and other di(chloroalkyl) amines. Among the alicyclic dichloroalkyl amines only a single example is mentioned in the literature [1].

In the present work we report the synthesis of some of the properties of dichloroalkylamines of the cyclopentane, cyclohexane, and cycloheptane series. We have synthesized compounds of two types: in one (I) the di(chloroalkyl)amine group is connected directly to a ring carbon, in the other to a carbon in the side chain (II).

$R-N(CH_2CH_2Cl)_2$ (I) $\qquad$ $R-CH_2N(CH_2CH_2Cl)_2$ (II)

R = cyclopentyl, cyclohexyl, cycloheptyl

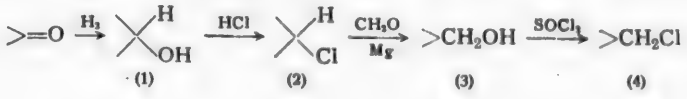
Compounds of type (II) are alicyclic derivatives of methyl N-bis-(chloroethyl)-amine (Soviet embichine) which has some value in oncology.

For the synthesis of N-di(chloroethyl)amines we have applied two very useful methods which differ from each other in the means of obtaining the intermediate N-di(hydroxyethyl)amine $RN(CH_2CH_2OH)_2$. In one process (a) (see Table 1), ethylene oxide acts on the amino compound; in the other (b) a halogen-containing compound is introduced into reaction with the diethanol amine. The conditions of carrying out the final step are the same for both methods; the replacement of the hydroxyl group by chlorine depends on the specific properties of N-di(hydroxyethyl)amine.

To obtain N-di(chloroethyl)amines of type (I) by method (b) the halogen in the alicyclic compound is not sufficiently reactive, since under various conditions, even including the use of high pressures, temperatures, and catalysts, only the starting halogen compound was recovered. Therefore the synthesis of dichloroalkylamines of this type was carried out by method (a). The required starting alkylamines were obtained in the cyclopentane and cycloheptane series by reducing the oximes of the corresponding ketones [2], and in the cyclohexane series by catalytic hydrogenation of the aromatic amino compounds. The hydrogenation was carried out in the presence either of Raney nickel or of platinum prepared by the Adams method. We hydrogenated aniline, p-aminobenzoic acid, its ethyl ester, m-aminobenzoic acid, and 1,3-phenylenediamine. The description of the hydrogenation of these compounds in the presence of nickel or platinum catalysts of different types is found in the literature [3], but in spite of this we had either to select the reaction conditions again or change the literature descriptions. When we hydrogenated in the presence of Raney nickel at high temperatures and pressures we found a cracking effect with liberation of ammonia. The amount of hydrogen absorbed usually exceeded the theoretical calculation. The yield of hydrogenated compounds was low. When we hydrogenated the same aromatic amino compounds in the presence of platinum (introduced into the reaction as platinum oxide), side reactions were not found. In the presence of a platinum catalyst we obtained ethyl 1,4-aminocyclohexanecarboxylate, 1,4- and 1,3-aminocyclohexanecarboxylic acids, and 1,3-cyclohexylenediamine. We did not attempt to determine the stearic

structure of these compounds and in further reactions we used the mixture of stereoisomers obtained by hydrogenation. The preparation of 1,3-cyclohexylenediamine allowed us to introduce two N-di(chloroethyl)amine groups into the cyclohexane molecule, which was of interest for the biological studies.

For carrying out the synthesis of compounds of type (II) we used as starting substances the chloromethyl derivatives of the same alicyclic hydrocarbons. The chloromethylcycloalkanes were obtained by thefollowing scheme.



(1) (2) (3) (4)

In the cyclopentane and cycloheptane series the syntheses were carried out beginning with the reduction of the ketone (1), in the cyclohexane series by obtaining chlorocyclohexane. Among the many and varied methods for reducing cyclopentanone [4] to cyclopentanol described in the literature the most suitable seemed to be hydrogenation in the presence of Raney nickel. The hydrogenation was carried out under more vigorous conditions than those of the literature; we used the same process for reduction of cycloheptanone. In this and other cases the cycloalkanols were obtained with yields of 67-87%. The remaining steps in the synthesis (2-3-4) were carried out as described in the literature [5]. In the cycloheptane series steps (3) and (4) were carried out for the first time. The reaction of replacement of chlorine by the di(hydroxyethyl)amine group in the chloromethylcycloalkanes by the action on them of diethanol amine was possible, but occurred only on long heating in a sealed tube and with addition of triethylamine to the reaction mixture. N-di (hydroxyethyl)amines, independent of their method of preparation, were in most cases introduced into the next reaction after one distillation in a vacuum.

The replacement of the hydroxyl by chlorine in N-di(hydroxyethyl)amines of both types (I and II) was carried out with thionyl chloride. This reaction occurred in the cold or at room temperature; heating caused strong tarring of the substances. The use of this method directly for 1,3- and 1,4-aminocyclohexanecarboxylic acids did not give good results, and so their di(chloroethyl) derivatives were obtained by saponifying the ethyl esters of 1,3- and 1,4-di(chloroethyl)aminocyclohexanecarboxylic acids. The latter were obtained in the usual way.

The N-di(chloroethyl)amines which we obtained are shown in Table 2 and the results of their biological study will be published in another place. According to preliminary results (A. I. Kravchenko) the most active and least toxic are the N-di(chloroalkyl)amines of the cycloheptane series, which certainly gives a reason for further search in this series for anti-cancer substances.

EXPERIMENTAL

Cyclohexylamine. In a rotating autoclave was placed 50 g of aniline and 10 g of Raney nickel,* the autoclave was filled with hydrogen to a pressure of 110 atm and heating was begun; at 160-170° and a hydrogen pressure of 140-150 atm rapid absorption of hydrogen occurred. After the corresponding treatment we obtained 16.85g (31%) of cyclohexylamine with b.p. 130-140°. The fraction which boiled above 140° crystallized on standing; the resulting substance melted at 90-100° which corresponds to the melting point of diphenylamine.

Ethyl 1,4-aminocyclohexanecarboxylate:** a) In the autoclave was placed 10 g of ethyl p-aminobenzoate hydrochloride, 150 ml of distilled water, and 1.5 g of platinum oxide. The autoclave was filled with hydrogen to a pressure of 50 atm and hydrogenation was carried out at room temperature (20°). At the end of the reaction the catalyst was separated, the water was distilled off in a vacuum, and the remaining substance was treated with a soda solution; the oil which separated was removed, dried and distilled in a vacuum, b. p. 125-135° (20-23 mm).

Found %: N 8.23. $C_9H_{17}O_2N$. Calculated %: N 8.17.

b) A mixture of 1,4-aminocyclohexanecarboxylic acid and a 15% ethyl alcohol solution of hydrogen chloride was heated. After the usual treatment we obtained the ethyl 1,4-aminocyclohexanecarboxylate with b.p. 125°

* The hydrogenation of aniline in the presence of nickel oxide is described in the literature [6].

** In the literature the hydrogenation of p-aminobenzoic and m-aminobenzoic acids in the presence of platinum is described. The hydrogenation is carried out without increased pressure [3].

(20 mm), $n^{20}D$ 1.4640. Yield 45%.

1,3-Aminocyclohexanecarboxylic acid and its ethyl ester. 6 g of m-aminobenzoic acid, 0.75 g of platinum oxide, and 80 ml of distilled water were placed in an autoclave for hydrogenation. Hydrogenation was carried out at room temperature; the original hydrogen pressure was 80 atm.

The reaction lasted for 4 hours. We obtained 6.44 g of substance with m.p. 251-252°. The substance was used without further purification for obtaining the ethyl ester.

The ethyl ester was obtained by heating 1,3-aminocyclohexanecarboxylic acid with a 15% solution of hydrogen chloride in anhydrous ethyl alcohol. B.p. 120-125° (15 mm), $n^{20}D$ 1.4640. Yield 75%.

Found %: C 62.88; H 10.03. $C_9H_{17}O_2N$. Calculated %: C 63.15; H 10.00.

1,3-Cyclohexylenediamine. In a rotating autoclave with a glass thermometric enclosure was placed 10.8 g of m-phenylenediamine dihydrochloride, 0.78 g of platinum oxide, and 45 ml of water. Hydrogenation was carried out at an initial hydrogen pressure of 50 or 60 atm and at room temperature (20°). Absorption of hydrogen lasted 15 hours and the amount absorbed corresponded to that calculated theoretically. After separation of the catalyst and evaporation of the solvent 34 g of calcium oxide and 123 ml of anhydrous alcohol were added to the residue and the reaction mixture was boiled; the alcohol was distilled off and the residue was repeatedly extracted with ethyl acetate. The ethyl acetate was distilled off and the residue distilled several times in a vacuum. We obtained about 2 g of substance with b.p. 97° (30 mm), $n^{20.5}D$ 1.5205.

Cycloheptanol* 50 g of cycloheptanone** in 100 ml of anhydrous methanol was hydrogenated in an autoclave at a hydrogen pressure of 60 atm and a temperature of 130-140° in the presence of 5 g of catalyst (Raney nickel). Hydrogen absorption lasted 2 hours. After separation of the catalyst and distillation of the alcohol the remaining substance was distilled in a vacuum. We obtained 25 g of cycloheptanol with b.p. 79-82° (12 mm).

Cycloheptyl carbinol. 4.4 g of chlorocycloheptane, 7.5 g of magnesium, and 30 ml of anhydrous ether were first heated with the addition of a little iodine and without stirring. After the reaction had begun, 33.6 g of chlorocycloheptane in 50 ml of ether was gradually added with stirring; when the reaction stopped at room temperature, it was heated for 15-20 minutes. Then, in a stream of nitrogen, 20 g of gaseous paraform was introduced. (The reaction took about half an hour.) Then the contents of the flask were poured on 150 g of ice and 57 ml of 30% sulfuric acid was carefully added. The cycloheptyl carbinol from the reaction mass was steam distilled off, separated, dried, and vacuum distilled, b.p. 84-94° (8-9 mm). We obtained 40 g.

Found %: C 75.00, 74.30; H 12.08, 12.57. $C_8H_{16}O$. Calculated %: C 75.00; H 12.50.

Chloromethylcycloheptane. To a mixture of 27 g of cycloheptyl carbinol and 20 ml of dry chloroform was added a solution of 35 ml of thionyl chloride in 20 ml of chloroform. The mixture was heated 3 hours at the boiling point. The excess thionyl chloride and chloroform were distilled off; the residue was vacuum distilled. We obtained 25 g of substance with b.p. 62-72° (8-10 mm). The substance was not purified more carefully.

Found %: Cl 21.0. $C_8H_{15}Cl$. Calculated %: Cl 24.2.

The substance was used without further purification of the next reaction with diethanol amine.

Preparation of N-di(β-hydroxyethyl)amines. a) A mixture of 1 mole of alicyclic amine and 2 moles of ethylene oxide was heated for 5 hours in a sealed tube in a rocking oven at 120-140°. A little mobile, thick oil was obtained which was either vacuum distilled or was used without distillation for the next reaction.

b) A mixture of 0.98 mole of diethanol amine, 1 mole of chloromethylcycloalkane, and 1 mole of triethylamine was heated 8-9 hours in a rocking oven in a sealed tube at 180-200°. At the end of the heating the N-di(hydroxyethyl)amine was extracted by ether, the ether solution was shaken with charcoal, and the ether was distilled off. The residue was vacuum distilled.

Preparation of N-di(β-chloroethyl)amines. A solution of 1 mole of N-di-(hydroxyethyl)amine and 6 moles of thionyl chloride in chloroform was stirred at room temperature for 8 hours, the thionyl chloride and chloroform

*Cycloheptanol was previously obtained from cycloheptanone by V. V. Markovnikov [7] by reduction with sodium and alcohol.

**Cycloheptanone was obtained by isomerization of cyclohexanone with diazomethane [8].

TABLE 1

R	Method of preparation	Empirical formula	Boiling point (pressure in mm)	Analysis (in %)					
				Calculated			Found		
				C	H	N	C	H	N
			$R—N(CH_2CH_2OH)_2$						
C_5H_9	a	$C_9H_{19}O_2N$	152—154° (6)	—	—	8.15	—	—	8.5
C_6H_{11}	a	$C_{10}H_{21}O_2N$	150 (15)	64.2	11.5	7.5	64.50	11.25	6.80
$C_6H_{10}(COOC_2H_5)$ (1,4)	a	$C_{13}H_{25}O_4N$	166—166.5 (0.25)	60.2	9.7	5.40	60.20	9.74	5.28
$C_6H_{10}(COOC_2H_5)$ (1,3)	a	$C_{13}H_{25}O_4N$	170—175 (4)	60.2	9.7	5.40	60.59	9.50	6.11
C_7H_{13}	a	$C_{11}H_{23}O_2N$	173—183 (4)	65.7	11.44	6.95	65.2	11.41	6.86
$C_7H_{13}—CH_2$	b	$C_{12}H_{25}O_2N$	140—180 (8—10)	67.0	11.6	6.52	65.87	11.29	6.32
			$R[N(CH_2CH_2OH)_2]_2$						
1,3-C_6H_{10}	a	$C_{14}H_{30}O_4N_2$	252—254 (11)	—	—	9.64	—	—	9.95

Note: Cyclopentylmethyl di(hydroxyethyl)amine $C_5H_9CH_2N(CH_2CH_2OH)_2$ and cyclohexylmethyl di(hydroxyethyl)amine were introduced into the following reactions without preliminary distillation and analysis.

TABLE 2

No.	R	Empirical formula	Melting point	Solvent for recrystallization	Analysis (in %)							
					Calculated				Found			
					C	H	N	Cl	C	H	N	Cl
				$R—N(CH_2CH_2Cl)_2 \cdot HCl$								
1	C_5H_9	$C_9H_{17}NCl_2 \cdot HCl$	106—107°	Benzene	43.8	7.3	5.7	43.2	43.64	7.00	5.75	43.48
2	C_6H_{11}	$C_{10}H_{19}NCl_2 \cdot HCl$	175—176	Acetone + + alcohol	46.05	7.67	5.37	40.87	45.90	7.63	5.50	40.65
3	$1,4\text{-}C_2H_5OOCC_6H_{10}$	$C_{13}H_{23}O_2NCl_2 \cdot HCl$	175—176	Benzene + + alcohol	46.95	7.27	4.21	32.0	47.09	7.44	4.37	32.28
4	$1,3\text{-}C_2H_5OCOC_6H_{10}$	$C_{13}H_{23}O_2NCl_2 \cdot HCl$	133—135	Benzene	46.95	7.27	4.21	32.00	47.14	7.2	4.77	33.39
5	$1,4\text{-}HOOC—C_6H_{10}$	$C_{11}H_{19}O_2NCl_2 \cdot HCl$	157—160	Anhydrous ether*	43.41	6.63	4.50	34.95	43.19	6.63	4.50	—
6	$1,3\text{-}HOOC—C_6H_{10}$	$C_{11}H_{19}O_2NCl_2 \cdot HCl$	68 (decomp.)	Anhydrous ether	43.41	6.63	4.50	34.95	42.96	6.65	4.61	35.06
7	C_7H_{13}	$C_{11}H_{21}NCl_2 \cdot HCl$	178	Benzene + + alcohol	48.2	8.04	5.1	38.8	48.11	7.92	5.01	38.51
8	$C_5H_9CH_2$	$C_{10}H_{19}NCl_2 \cdot HCl$	128—130	Ethyl acetate	46.1	7.69	5.38	40.8	45.99	7.79	5.70	40.4
9	$C_6H_{11}CH_2$	$C_{11}H_{21}NCl_2 \cdot HCl$	145—147	Benzene + + alcohol	48.2	8.04	5.1	38.8	48.12	7.73	5.04	38.66
10	$C_7H_{13}CH_2$	$C_{12}H_{23}NCl_2 \cdot HCl$	141—143	Benzene + + alcohol	49.8	8.32	4.85	37.0	49.57	8.25	4.84	36.32
				$R[N(CH_2CH_2Cl)_2]_2 \cdot 2HCl$								
11	$1,3\text{-}C_6H_{10}$	$C_{14}H_{28}N_2Cl_4 \cdot 2HCl$	101	Chloroform **	38.5	6.47	6.41	48.70	39.37	6.69	7.00	46. 13

*Substances 5 and 6 were purified by washing with anhydrous ether and drying in a vacuum desiccator over phosphorus pentoxide.

**Purification of this substance was carried out by boiling its chloroform solution with charcoal and after separating the charcoal, distilling the solvent.

were distilled off in a vacuum, and the residue was recrystallized from organic solvents. The N-di(hydroxyethyl)amines and N-di(chloroethyl)amine hydrochlorides which were obtained are shown in Tables 1 and 2.

Preparation of 1,3- and 1,4-N-di(chloroethyl)aminocyclohexanecarboxylic acids. The ethyl esters of the N-di(chloroethyl)aminocyclohexanecarboxylic acids were heated with excess concentrated hydrochloric acid at 120-130° for 3 hours. The cooled solutions were treated with activated charcoal until decolorized and the hydrochloric acid was distilled off in a vacuum. Repeated additions of anhydrous ether and its distillation removed the residual hydrogen chloride. The product was dried in a vacuum desiccator over phosphorus pentoxide.

SUMMARY

1) We have obtained N-di(chloroethyl)amine hydrochlorides of the alicyclic series.

2) We have described methods for obtaining some starting and intermediate substances.

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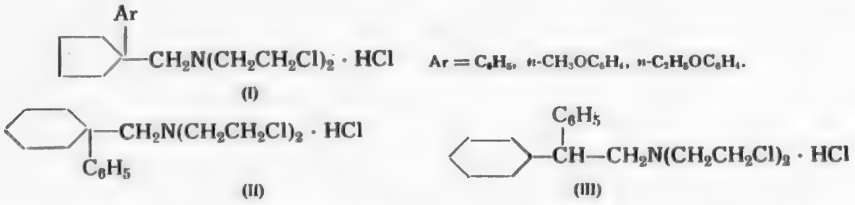
N-DI(CHLOROETHYL)AMINES WITH ALICYCLIC AND AROMATIC RADICALS IN THE MOLECULE. II.

S. I. Sergievskaia, K. V. Levshina, A. I. Gavrilova and A. K. Chizhov

The purpose of our study was to obtain N-di(chloroethyl)amines which contained in their molecule both aromatic and alicyclic radicals at the same time. The structure of these compounds is shown in the following scheme.



Compounds of types (I) and (II) are the arylated analogs of some N-di(chloroethyl)amines of the alicyclic series described in the preceding paper [1]. Compound (III) is distinguished from (I) and (II) by the fact that the aromatic radical in it is not a component part of the alicyclic radical.

To obtain these compounds we used as the starting substances the corresponding cyanides: for the synthesis of compounds of types (I) and (II), nitriles of the structure ArR—CN, for compound (III), the nitrile R—CH—CN, where
|
C_6H_5

R is the alicyclic radical. All these nitriles are easily obtained by condensing benzyl cyanide with the bromides (1,4-dibromobutane, 1,5-dibromopentane, and bromocyclohexane) in the presence of sodium amide. Among the nitriles which we thus obtained, only 1-(p-ethoxyphenyl)-1-cyanocyclopentane has not been described in the literature.

Reduction of the nitriles to the primary amines was carried out either by catalytic hydrogenation in the presence of Raney nickel, or with lithium aluminum hydride. Transformation of the amine to its N-di(hydroxyethyl) derivative and from the latter to the corresponding N-di(chloroethyl)amine was carried out by the method described in our previous paper [1].

Difficulty was encountered in the purification of the N-di(chloroethyl)amine hydrochlorides which contained the cyclohexyl radical: 1-(phenylcyclohexyl)-1-methyl-N-di(chloroethyl)amine hydrochloride was unstable and one atom of chlorine in it was quickly replaced by a hydroxyl group; therefore in the choice of solvents and in recrystallization a number of precautions had to be observed. It was also difficult to purify (β-phenyl-β-cyclohexyl)-ethyl-N-di(chloroethyl)-amine hydrochloride.

According to the preliminary results of the biological study, the introduction of the phenyl group in the molecule in these cases does not have a favorable effect on the anti-cancer activity of the compounds.

EXPERIMENTAL

1-(p-Ethoxyphenyl)-1-cyanocyclopentane $C_5H_8(C_6H_4OC_2H_5)CN$. To 10 g of sodium amide in 100 ml of anhydrous toluene was gradually added 18.15 g of p-ethoxybenzyl cyanide in 65 ml of anhydrous toluene. The reaction mixture was heated on the boiling water bath until evolution of ammonia stopped, and then 24.4 g of 1,4-dibromobutane was added at such a rate that the temperature did not rise above 50°, after which the mixture was heated for 15 hours. After the mixture had cooled it was decomposed with 50 ml of water, the toluene layer was separated, the water was repeatedly extracted with toluene, and the toluene solutions were combined. After the toluene solution had been dried the toluene was distilled off and the residue distilled in a vacuum. B.p. 135-140° (0.3-0.4 mm).

Found %: N 6.47. $C_{14}H_{18}ON$. Calculated %: N 6.5.

In an analogous manner the previously described compounds were obtained: 1-(phenyl)-1-cyanocyclopentane [2], 1-(p-methoxyphenyl)-1-cyanocyclopentane [3], 1-(phenyl)-1-cyanocyclohexane [4], and the nitrile of phenylcyclohexyl acetic acid [5].

1-Phenyl-1-aminomethylcyclopentane $C_6H_5-C_5H_8-CH_2NH_2$. 50 g of 1-phenyl-1-cyanocyclopentane in solution in 200 ml of anhydrous methanol previously saturated with ammonia was hydrogenated in the presence of a skeletal nickel catalyst at 110-120° for 3.5 hours at an initial hydrogen pressure of 100 atm. After the catalyst had been removed and the solvent distilled, the residue was distilled in a vacuum. We collected the fraction with b.p. 129-130° (7 mm). Yield 43.44 g (85%). The substance was strongly basic and in air absorbed carbon dioxide.

The hydrochloride was obtained by the action of an ether solution of hydrogen chloride on an ether solution of the amine. White, crystalline substance. After recrystallization from anhydrous ethyl acetate it melted at 223-224°.

Found %: Cl 17.85, 17.72; N 7.07, 6.92. $C_{12}H_{15}NH_2 \cdot HCl$. Calculated %: Cl 17.9; N 7.1.

1-(p-Methoxyphenyl)- and 1-(p-ethoxyphenyl)-aminomethylcyclopentanes. To 0.47 mole of $LiAlH_4$ in 50 ml of anhydrous ether was added with stirring 0.027 mole of 1-(p-alkoxyphenyl)-1-cyanocyclopentane in 50 ml of anhydrous ether at such a speed that the reaction mass boiled weakly. After the addition of all the nitrile, the reaction mass was heated for 1 hour at the temperature of boiling ether. Then a small amount of water was carefully added to decompose the excess $LiAlH_4$ and 60 ml of 20% sodium hydroxide solution was added. The ether layer was separated and the water was extracted by ether; the combined ether solutions were dried over potassium hydroxide. The ether was distilled off and the residue vacuum distilled. The yield of 1-(p-alkoxyphenyl)-1-aminomethylcyclopentane was 90-95%.

The hydrochlorides of these amines were obtained by the action of an ether solution of hydrogen chloride on an ether solution of the amine. B.p. of 1-(p-methoxyphenyl)-1-aminomethylcyclopentane was 125-130° (3 mm). Its hydrochloride after recrystallization from anhydrous ethyl acetate melted at 174-175°.

Found %: C 64.26; H 8.11; Cl 14.7. $C_{13}H_{19}ON \cdot HCl$. Calculated %: C 64.60; H 8.30; Cl 15.01.

The boiling point of the fraction which contained chiefly 1-(p-ethoxyphenyl)-1-aminomethylcyclopentane was 115-130° (2 mm). Its hydrochloride melted after recrystallization from anhydrous ethyl acetate at 142-143°.

Found %: C 65.80; H 8.89; N 5.58; Cl 13.97. $C_{14}H_{21}ON \cdot HCl$. Calculated %: C 65.90; H 8.67; N 5.50; Cl 13.90.

1-Phenyl-1-aminomethylcyclohexane. $(C_6H_5)C_6H_{10}CH_2NH_2$. To a mixture of 2.93 g of lithium aluminum hydride and 155 ml of anhydrous ether was added dropwise a solution of 8.58 g of 1-phenyl-1-cyanocyclohexane in 20 ml of anhydrous ether. At the end of the reaction aqueous alkali was gradually added to the cooled reaction mixture. The further treatment was the same as previously described. We obtained 8.01 g (91.2%) of 1-phenyl-1-aminomethylcyclohexane.

B.p. 127.5-128° (3.5 mm), 129.5-131.1° (4 mm), $n^{20}D$ 1.5462.
Found %: C 82.74; H 10.10; N 7.57. $C_{13}H_{19}N$. Calculated %: C 82.50; H 10.10; N 7.40.

β-Phenyl-β-cyclohexylethylamine. $C_6H_5CH(C_6H_{11})CH_2NH_2$. 28.3 g of the nitrile of phenylcyclohexylacetic acid [5], 440 ml of 19.6% ammonia solution in methyl alcohol, and 17.5 g of skeletal nickel catalyst were placed in an autoclave and hydrogenated. (The initial hydrogen pressure at 20° was 77 atm.) The reaction mixture was heated to 120° and kept at this temperature for 3.5 hours. After the usual treatment of the reaction mixture and vacuum distillation of the methyl alcohol, the residue was vacuum distilled. We obtained a substance with b.p. 145° (5 mm); 122.5-123.5° (3 mm). The yield was nearly quantitative.

Found %: N 6.57. $C_{14}H_{21}N$. Calculated %: N 6.88.

N-di(hydroxyethyl)amines were obtained by heating the corresponding amine with ethylene oxide in a sealed tube at 130-140° for 3-6 hours. After 2 vacuum distillations they were used for the following reaction.

We obtained the following compounds.

1. (Phenylcyclopentyl)-methyl-N-di(hydroxyethyl)amine

$$(C_6H_5C_5H_8)CH_2N(CH_2CH_2OH)_2,$$

b.p. 224-227° (8 mm). Yield 93.5%.

2. (p-Methoxyphenylcyclopentyl)methyl-N-di(hydroxyethyl)amine, b.p. 195-210° (3 mm). Yield 80.4%.

3. (p-Ethoxyphenylcyclopentyl)methyl-N-di(hydroxyethyl)amine, b.p. 195-200° (3 mm). Yield 68.2%.

Found %: C 69.80; H 9.29; N 4.44. $C_{19}H_{29}O_3N$. Calculated %: C 70.04; H 9.45; N 4.56.

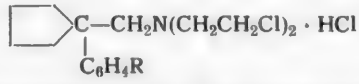
4. (Phenylcyclohexyl)methyl-N-di(hydroxyethyl)amine, b.p. 161.5-162° (1 mm). Yield 89.7%. n_D^{20} 1.5443.

Found %: C 73.84; H 9.57; N 5.17. $C_{17}H_{27}O_2N$. Calculated %: C 73.60; H 9.81; N 5.06.

5. (β-Phenyl-β-cyclohexyl)ethyl-N-di(hydroxyethyl)amine, b.p. 192-195° (2.5 mm), $n^{20}D$ 1.5330.

Found %: C 74.08. H 10.08. $C_{18}H_{29}O_2N$. Calculated %: C 74.08; H 10.03.

N-di(chloroethyl)amines. a) N-di(chloroethyl)amines which contain the cyclopentyl radical were obtained from the corresponding N-di(hydroxyethyl)amines by the action of thionyl chloride on them. The reaction was carried out in chloroform solution at room temperature and the amines were obtained as their hydrochlorides. In most cases these were recrystallized from ethyl acetate; in the case of (p-methoxyphenylcyclopentyl)methyl-N-di(chloroethyl)amine hydrochloride, the substance was first dissolved in benzene and was precipitated from the benzene by anhydrous ether, and only after this purification was recrystallized from ethyl acetate. The N-di-(chloroethyl)amine hydrochlorides of this series are shown in the Table.



R	Melting point	Calculated (%)				Found (%)			
		C	H	N	Cl	C	H	N	Cl
H	157—158°	57.10	7.15	4.15	31.6	57.14	7.20	4.10	31.7
OCH_3	128—129	55.80	7.10	3.82	29.1	55.90	7.37	3.77	—
OC_2H_5	138—140	56.75	7.36	3.68	28.1	57.02	7.28	3.73	—

b) (1-Phenylcyclohexyl-1)methyl-N-di(chloroethyl)amine hydrochloride. The reaction of phenylcyclohexylmethyl-N-di(hydroxyethyl)amine (11.75 g) with thionyl chloride (7.22 ml) was carried out in a solution of anhydrous chloroform (35 ml) at 70-80°. After the chloroform and thionyl chloride had been distilled off in a vacuum, anhydrous benzene was added to the residue and it was distilled off in a vacuum; this operation was repeated several times. We obtained a crystalline precipitate (1.89 g) with m.p. 123-127°. After recrystallization from anhydrous benzene the substance melted at 123-125°. According to the analysis, the chlorine content

of the substance was low, but the presence of a hydroxyl group was not detected.

Found %: Cl 28.57. $C_{17}H_{26}NCl_2 \cdot HCl$. Calculated %: Cl 30.38.

If the substance with m.p. 123-127° was recrystallized from anhydrous acetone or a mixture of alcohol and ether, we obtained a substance with m.p. 190-200°. The analysis of this substance showed that its composition was close to that of phenylcyclohexylmethyl-N-(hydroxyethyl) (chloroethyl)amine hydrochloride.

(β-Phenyl-β-cyclohexyl)ethyl-N-di(chloroethyl)amine. A mixture of 6.93 g of (β-phenyl-β-cyclohexyl) ethyl-N-di(hydroxyethyl)amine, 32 ml of chloroform, and 51.74 g of thionyl chloride was heated at 70° for 3 hours. Further treatment was the same as in the previous experiment. The resulting colored oil was treated with an excess of 50% solution of potash and the oil which formed was extracted with ether. After distilling off the ether we collected a substance with b.p. 168-179° (0.15 mm).

Found %: C 65.61, 65.38; H 8.13, 8.00; Cl 21.57. $C_{18}H_{27}NCl_2$. Calculated %: C 65.82; H 8.29; Cl 21.60.

The hydrochloride was obtained by the action of an ether solution of hydrogen chloride on the above base. It was purified by careful washing with anhydrous ether. We did not obtain the melting point since the substance decomposed when it was heated; it was easily soluble in water.

Found %: C 59.52; H 8.21. $C_{18}H_{27}NCl_2 \cdot HCl$. Calculated % C 59.30; H 7.73.

SUMMARY

1. We have synthesized N-di(chloroethyl)amines which have not been described in the literature and also some other compounds of the cyclopentane and cyclohexanes series.

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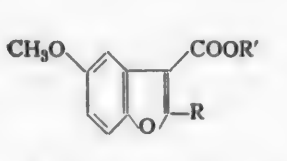
THE ALKYLATION OF SUBSTITUTED 5-HYDROXYBENZOFURANS; SYNTHESIS OF NEW PLANT GROWTH STIMULANTS

A. N. Grinev, N. K. Venevtseva and A. P. Terent'ev

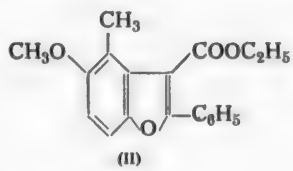
We have succeeded in working out a method of synthesis of substituted 5-hydroxybenzofurans by condensation of p-quinones with esters of β-ketoacids [1-5]. These investigations permitted getting a series of 5-hydroxybenzofuran derivatives. In order to show the structure of the resulting compounds, we have already in our work methylated some of them with dimethyl sulfate, and depending on the reaction conditions we have obtained either derivatives of 5-methoxybenzofuran-3-carboxylic acid [3, 5], or esters of the latter [6].

In the present work, by reaction of 5-hydroxybenzofurans with dimethyl sulfate in an alkaline medium in the presence of dioxane, we have obtained 2-phenyl-3-carbethoxy-5-methoxybenzofuran (I), 2-phenyl-3-carbethoxy-4-methyl-5-methoxybenzofuran (II), 2-phenyl-3-carbethoxy-5-methoxy-6-methylbenzofuran (III), 2-(p-nitrophenyl)-3-carbethoxy-5-methoxybenzofuran (IV), 2-methyl-3-carbethoxy-5-methoxy-6,7-dichlorobenzofuran (V), and 2-phenyl-3-carbethoxy-5-methoxy-6,7-dichlorobenzofuran (VI).

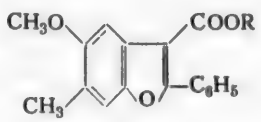
By hydrolysis of the esters (I), (III), (V) and (V) with alcoholic alkali we have obtained 2-phenyl-3-carboxy-5-methoxybenzofuran (VII), 2-phenyl-3-carboxy-5-methoxy-6-methylbenzofuran (VIII), 2-methyl-3-carboxy-5-methoxy-6,7-dichlorobenzofuran (IX), and 2-phenyl-3-carboxy-5-methoxy-6,7-dichlorobenzofuran (X). As a result of alkylation of the earlier synthesized hydroxyacids of the benzofuran chloroacetic acid series, we have obtained 2-methyl-3-carboxy-6,7-dichlorobenzofuran-5-hydroxyacetic acid (XI), and 2-phenyl-3-carboxy-6,7-dichlorobenzofuran-5-hydroxyacetic acid (XII)



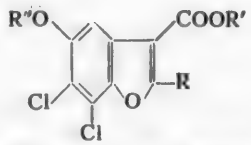
(I) $R = C_6H_5$, $R' = C_2H_5$;
(IV) $R = p\text{-}C_6H_4NO_2$, $R' = C_2H_5$
(VII) $R = C_6H_5$, $R' = H$;



(II)



(III) $R = C_2H_5$.
(VIII) $R = H$.



(V) $R = CH_3$, $R' = C_2H_5$, $R'' = CH_3$; (X) $R = C_6H_5$, $R' = H$, $R'' = CH_3$;
(VI) $R = C_6H_5$, $R' = C_2H_5$, $R'' = CH_3$; (XI) $R = CH_3$, $R' = H$, $R'' = CH_2COOH$;
(XI) $R = CH_3$, $R' = H$, $R'' = CH_3$; (XII) $R = C_6H_5$, $R' = H$, $R'' = CH_2COOH$.

The potassium salts of acids (VII-XII), tested in the Botanical Garden of Moscow State University by N. A. Bazilevskaia, were very effective stimulants for the growth of plants. The results of the biological study of these compounds will be published separately.

EXPERIMENTAL

2-Phenyl-3-carbethoxy-5-methoxybenzofuran (I). 102 g of 2-phenyl-3-carbethoxy-5-hydroxybenzofuran with m.p. 154-155° [5] was dissolved in 200 ml of dioxane and the resulting solution was treated with 500 ml of 2 N sodium hydroxide (the solution became light green) and then with 100 ml of dimethyl sulfate. The reaction solution was shaken in a closed, thick walled vessel at room temperature for 35-40 minutes, diluted with 2-3 volumes of water, and well cooled. Crystals of 2-phenyl-3-carbethoxy-5-methoxybenzofuran (I) separated and were recrystallized from alcohol. Yield 95 g, m.p. 59-60°.

Found %: C 73.48, 73.52; H 5.60, 5.58. $C_{18}H_{16}O_4$. Calculated %: C 72.96; H 5.44.

2-Phenyl-3-carbethoxy -4-methyl-5-methoxybenzofuran (II). The reaction was carried out under the conditions of the preceding experiment. We took 28 g of 2-phenyl-3-carbethoxy-4-methyl-5-hydroxybenzofuran with m.p. 143-144° [2], 20 ml of dimethyl sulfate, 100 ml of 2 N sodium hydroxide, and 100 ml of dioxane. The yield of (II) was 28.8 g, m.p. 77-78° (from a mixture of alcohol and dioxane, 5 : 1)

Found %: C 74.15, 73.98; H 5.99, 6.09. $C_{19}H_{18}O_4$. Calculated %: C 73.53; H 5.85.

2-Phenyl-3-carbethoxy-5-methoxy-6-methylbenzofuran (III). For the experiment we took 85 g of 2-phenyl-3-carbethoxy-5-hydroxy-6-methylbenzofuran with m.p. 188-189° [2], 60 ml of dimethyl sulfate, 300 ml of 2 N sodium hydroxide, and 200 ml of dioxane. All the operations were carried out in the same way as in preparing (I). The yield of (III) was 90 g, m.p. 72-73° (from a mixture of alcohol and dioxane, 10 : 1).

Found %: C 73.64, 73.91; H 6.02, 6.03. $C_{19}H_{18}O_4$. Calculated %: C 73.53; H 5.85.

2-(p-Nitrophenyl)-3-carbethoxy-5-methoxybenzofuran (IV). For the experiment we took 3 g of 2-(p-nitrophenyl)-3-carbethoxy-5-hydroxybenzofuran with m.p. 208-210° [4], 2 ml of dimethyl sulfate, 10 ml of 2 N sodium hydroxide, and 15 ml of dioxane. All the operations were carried out as in the previous experiments. The yield of (IV) was 2.8 g, m.p. 167° (from a mixture of alcohol and dioxane, 1 : 2).

Found %: C 63.44, 63.48; H 4.66, 4.66. $C_{18}H_{15}O_6N$. Calculated %: C 63.34; H 4.43.

2-Methyl-3-carbethoxy-5-methoxy-6,7-dichlorobenzofuran (V). For the experiment we took 4.2 g of 2-methyl-3-carbethoxy-5-hydroxy-6,7-dichlorobenzofuran with m.p. 202.5° [1], 3 ml of dimethyl sulfate, 15 ml of 1 N sodium hydroxide and 28 ml of dioxane. All the operations were the same as before. Yield of (V), 4.1 g, m.p. 124-125° (from a mixture of ethyl alcohol and dioxane, 3 : 1).

Found %: C 51.95, 51.91; H 4.06, 4.12. $C_{13}H_{12}O_4Cl_2$. Calculated %: C 51.54; H 3.99.

2-Phenyl-3-carbethoxy-5-methoxy-6,7-dichlorobenzofuran (VI). For the experiment we took 4.2 g of 2-phenyl-3-carbethoxy-5-hydroxy-6,7-dichlorobenzofuran with m.p. 185-186° [1], 2.4 ml of dimethyl sulfate, 12.5 ml of 2 N sodium hydroxide, and 15 ml of dioxane. All the operations were carried out as in the previous experiments. Yield of (VI), 4 g, m.p. 149-150° (from a mixture of ethyl alcohol with dioxane, 1 : 1).

Found %: C 56.53, 56.68; H 3.99, 3.97. $C_{18}H_{14}O_4Cl_2$. Calculated %: C 56.46; H 3.86.

2-Phenyl-3-carboxy-5-methoxybenzofuran (VII). 18 g of sodium hydroxide was dissolved in 200 ml of alcohol, and 45 g of ester (I) was added to the resulting solution. The reaction mixture was heated to boiling under reflux for 45 minutes, diluted with 200 ml of water, and filtered. Acidification of the filtrate with concentrated hydrochloric acid (to Congo) precipitated acid (VII). Yield 40 g, m.p. 176-177° (from acetic acid). A mixed melting point with an earlier preparation of compound (VII) [5] gave no depression.

2-Phenyl-3-carboxy-5-methoxy-6-methylbenzofuran (VIII). For the experiment we took 47 g of ester (III), 20 g of sodium hydroxide, and 170 ml of alcohol. All the operations were carried out as in the previous experiment. Yield of (VIII) 40.5 g, m.p. 200-201° (from aqueous acetic acid.

Found %: C 72.63, 72.82; H 5.20, 5.27. $C_{17}H_{14}O_4$. Calculated %: C 72.33; H 5.00.

2-Methyl-3-carboxy-5-methoxy-6,7-dichlorobenzofuran (IX). For the experiment we took 3 g of ester (V), 1.2 g of sodium hydroxide, and 25 ml of alcohol. All operations were carried out as in the preparation of (VII). Yield of (IX) 2.5 g, melts with decomposition at 319.5-321° (from acetic acid).

Found %: C 48.28, 48.49; H 3.07, 3.08. $C_{11}H_8O_4Cl_2$. Calculated %: C 48.02; H 2.97.

2-Phenyl-3-carboxy-5-methoxy-6,7-dichlorobenzofuran (X). For the experiment we took 2.8 g of ester (VI), 1.2 g of sodium hydroxide, and 25 ml of alcohol. All the operations were the same as before. Yield 2.4 g, m.p. 298-300° (from acetic acid).

Found %: C 56.63, 56.46; H 3.13, 3.15. $C_{16}H_{10}O_4Cl_2$. Calculated %: C 56.99; H 2.99.

2-Methyl-3-carboxy-6,7-dichlorobenzofuran-5-hydroxyacetic acid (XI). To a solution of 7.9 g of 2-methyl-3-carboxy-5-hydroxy-6,7-dichlorobenzofuran with m.p. 275-278° [1] in 14 ml of 40% sodium hydroxide solution was added 12 ml of 50% solution of monochloroacetic acid in water, and then 30 ml more of water. The reaction mixture was heated for 1 hour on the water bath. The sodium salt of acid (XI) was precipitated from the solution in the usual way. Yield of (XI) 8.5 g, m.p. above 260° (with decomposition).

Found %: C 42.62, 42.64 H 3.21, 3.37. $C_{12}H_{10}O_7Cl_2$. Calculated %: C 42.75; H 2.99.

2-Phenyl-3-carboxy-6,7-dichlorobenzofuran-5-hydroxyacetic acid (XII). To 3.5 g of 2-phenyl-3-carboxy-5-hydroxy-6,7-dichlorobenzofuran with m.p. 207° [1] was added 3.7 ml of 40% sodium hydroxide and ethyl alcohol to full solution of the precipitate. To the resulting solution was added 4 ml of 50% aqueous solution of monochloric acid. Further operations were carried out as in the previous experiment. Yield of (XII) 4 g (96.8), m.p. 288-289° (from acetic acid).

Found %: C 53.98, 54.05; H 2.89, 2.91. $C_{17}H_{10}O_6Cl_2$. Calculated %: C 53.56; H 2.64.

SUMMARY

1. We have worked out a method for alkylating derivatives of 5-hydroxybenzofuran by the action of dimethyl sulfate on them.

2. By the reaction of 5-hydroxybenzofurans with chloroacetic acid we have obtained analogs of phenoxyacetic acid.

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A NEW METHOD FOR OBTAINING SUBSTITUTED BENZOFURANS AND INDOLES FROM ESTERS OF BENZOFURAN- AND INDOLE-β-CARBOXYLIC ACIDS

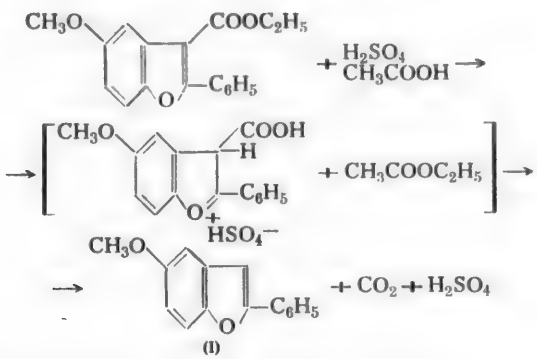
A. N. Grinev, I. A. Zaitsev, N. K. Venevtseva and A. P. Terent'ev

In a large number of cases esters of substituted benzofuran- and indole-β-carboxylic acids are more accessible than the benzofurans and indoles themselves. The carboxyl group in these compounds is held firmly enough, and its splitting off requires severe conditions which unavoidably lead to considerable loss of the substance [1, 2].

We have frequently had to carry out the removal of carboxyl groups in a number of substituted benzofuran-, benzodifuran-, and indole-β-carboxylic acids [3,6]. 2,6-Dimethyl- and 2,4,6-trimethylbenzo(1,2-b; 4,5-b')-difuran-3,7-dicarboxylic acids lose both carboxyls when heated with quinoline in the presence of copper oxide [3], but for the decarboxylation of benzofuran- and indole-β-carboxylic acids this process is not suitable. Some substituted benzofuran-β-carboxylic acids have been transformed into benzofurans in yields of about 50% by heating with calcium oxide [4, 5], but when other benzofuran acids of this type were decarboxylated by this method the yields of benzofurans were very small. We obtained 2-methyl-5-methoxyindole by heating 2-methyl-3-carboxy-5-methoxyindole to 140° in glycerine with a yield of 85% [6].

However, up to now we have not succeeded in carrying out the synthesis of N-alkyl or N-aryl substituted indoles with free β-positions by these or other processes.

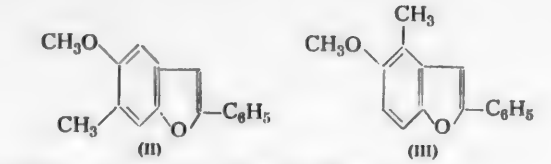
In the present work we give a number of examples of a successful method of splitting esters of benzofuran- and indole-β-carboxylic acids by heating them with equimolecular amounts of sulfuric or phosphoric acids in glacial acetic acid. The reaction goes by the following scheme



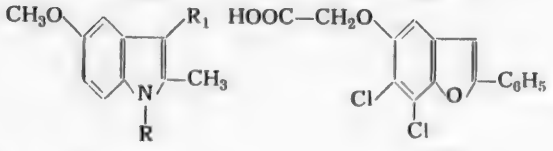
(I)

By splitting the corresponding esters with sulfuric acid in glacial acetic acid we obtained 2-phenyl-5-methoxybenzofuran (I), 2-phenyl-5-methoxy-6-methylbenzofuran (II), 2-phenyl-4-methyl-5-methoxybenzofuran (III), and 1,2-dimethyl-5-methoxyindole (IV), and by reaction with phosphoric acid, 1-phenyl-2-methyl-3-carbethoxy-5-methoxyindole (V) gave 1-phenyl-2-methyl-5-methoxyindole (VI).

2-Phenyl-3-carboxy-6,7-dichlorobenzofuran-5-hydroxyacetic acid was also split by sulfuric acid; it gave 2-phenyl-6,7-dichlorobenzofuran-5-hydroxyacetic acid (VII).



(II) (III)



(IV) $R = CH_3$, $R_1 = H$;
(V) $R = C_6H_5$, $R_1 = COOC_2H_5$;
(VI) $R = C_6H_5$, $R_1 = H$.

(VII)

EXPERIMENTAL

1. Preparation of 2-phenyl-5-methoxybenzofuran (I). 5 g of 2-phenyl-3-carbethoxy-5-methoxybenzofuran with m.p. 59-60° [7] was dissolved in 25 ml of acetic acid and 5 ml of concentrated sulfuric acid was added to the resulting solution. The reaction mixture was heated for 1 hour at the boiling point and then cooled; the crystals which precipitated were separated and recrystallized from acetic acid. Yield of (I), 3 g (79.5%), m.p. 127°.

Found %: 80.36, 80.45; H 5.56, 5.49. $C_{15}H_{12}O_2$. Calculated %: C 80.33; H 5.39.

2. Preparation of 2-phenyl-5-methoxy-6-methylbenzofuran (II). For the reaction we took 9.2 g of 2-phenyl-3-carbethoxy-5-methoxy-6-methylbenzofuran with m.p. 72-73° [7], 46 ml of acetic acid, and 9.2 ml of concentrated sulfuric acid. Reaction and treatment were carried out as in experiment 1. Yield of (II), 6.5 g (91.5%), m.p. 150-150.5°.

Found %: C 80.65, 80.83; H 5.96, 6.08. $C_{16}H_{14}O_2$. Calculated %: C 80.64, H 5.92.

3. Preparation of 2-phenyl-4-methyl-5-methoxybenzofuran (III). For the reaction we used 13 g of 2-phenyl-3-carbethoxy-4-methyl-5-methoxybenzofuran with m.p. 77-78° [7], 65 ml of acetic acid, and 12 ml of concentrated sulfuric acid. Yield of (III), 9 g (90%), m.p. 79°.

Found %: C 80.90, 80.85; H 6.10, 6.18. $C_{16}H_{14}O_2$. Calculated %: C 80.64, H 5.92.

4. Preparation of 1,2-dimethyl-5-methoxyindole (IV). For the reaction we took 9.2 g of 1,2-dimethyl-3-carbethoxy-5-methoxyindole with m.p. 114-115° [8], 50 ml of acetic acid, and 10 ml of concentrated sulfuric acid. The reaction mixture was heated to boiling for 30 minutes, cooled, and neutralized with 2 N sodium hydroxide, and then steam distilled. Yield of (IV), 4.2 g (64.5%), m.p. 67-68°.

Found %: C 75.68, 75.86; H 7.70, 7.51. $C_{11}H_{13}ON$. Calculated %: C 75.40; H 7.48.

5. Preparation of 1-phenyl-2-methyl-3-carbethoxy-5-methoxyindole (V). For the reaction we used 32 g of 1-phenyl-2-methyl-3-carbethoxy-5-hydroxyindole with m.p. 205-206° [9], 28 g of dimethyl sulfate, 100 ml of 2 N sodium hydroxide, and 100 ml of dioxane. The reaction was carried out under the conditions for methylation of the 5-hydroxy substituted benzofurans [7]. The yield of (V) was 25.4 g (75.8%), m.p. 88-90° (from methanol).

Found %: C 74.22, 74.12; H 6.41, 6.39. $C_{19}H_{19}O_3N$. Calculated %: C 73.76; H 6.19.

6. Preparation of 1-phenyl-2-methyl-5-methoxyindole (VI). For the reaction we took 5.6 g of 1-phenyl-2-methyl-3-carbethoxy-5-methoxyindole, 20 ml of acetic acid, and 5 ml of concentrated phosphoric acid. The reaction mixture was heated to boiling for 1 hour, cooled, and neutralized for 2 N sodium hydroxide. The oil which precipitated crystallized when it stood for a week. The crystals were separated and recrystallized from benzine. Yield of (VI), 2.8 g (65.3%), m.p. 79-80°.

Found %: C 81.32, 81.25; H 6.17, 6.13. $C_{16}H_{15}ON$. Calculated %: C 80.98; H 6.37.

7. Preparation of 2-phenyl-6,7-dichlorobenzofuran-5-hydroxyacetic acid (VII). For the reaction we took 4.5 g of 2-phenyl-3-carboxy — 6,7-dichlorobenzofuran-5-hydroxyacetic acid with m.p. 288-289° [7], 45 ml of acetic acid, and 9 ml of concentrated sulfuric acid. The reaction mixture was boiled for 2 hours (to full solution of the precipitate). The resulting solution was diluted with water. The crystals which precipitated were separated, dried, and recrystallized from ethyl alcohol. Yield of (VII), 3.3 g (83.6%). A mixed melting point of the resulting preparation and 2-phenyl-3-carboxy-5-methoxy-6,7-dichlorobenzofuran [7] melted at 246-265°.

Found %: C 57.26, 57.12; H 3.22, 3.12. $C_{16}H_{10}O_4Cl_2$. Calculated %: C 56.99; H 2.99.

SUMMARY

We have worked out a new method for preparing benzofurans and indoles from esters of benzofuran- and indole-β-carboxylic acids.

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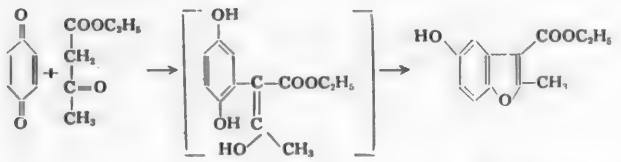
STUDIES IN THE FIELD OF QUINONES

XXIII. STUDIES OF THE CONDENSATION OF p-BENZOQUINONE AND 2,3-DICHLOROQUINONE WITH ACETOACETIC ESTER AND ITS ANALOGS

A. N. Grinev, N. K. Venevtseva and A. P. Terent'ev

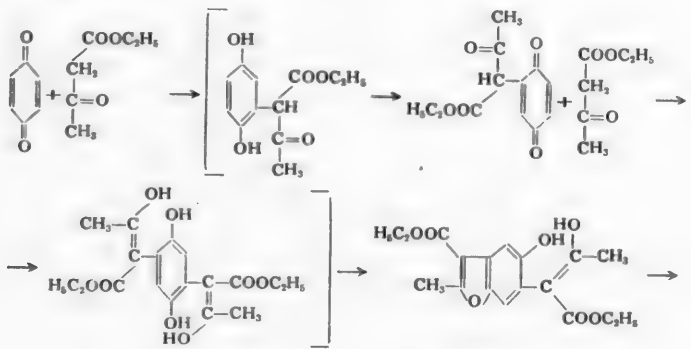
p-Benzoquinone, as has already been shown [1-5], reacts with acetoacetic and benzoylacetic esters, and if the reaction is carried out above 80°, depending on the concentration of p-benzoquinone in the reaction mixture, there is formed either mostly benzodifuran derivatives [1, 2, 4], or exclusively substituted benzofurans [3-5].

In the present work we have carried out the condensation of p-benzoquinone with acetoacetic ester at lower temperatures. These studies lead to results which differ from those obtained in the previous work. If the reaction between p-benzoquinone and acetoacetic ester proceeds at 80-85° and low concentrations of p-benzoquinone in the reaction mixture, the chief product (and with very small concentrations of p-benzoquinone, the only one) is benzofuran (I) [2, 3].

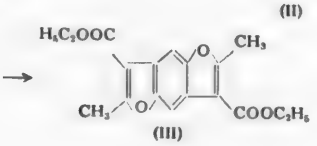


(I)

At 41-45° and also at low concentrations of p-benzoquinone in the reaction mixture there are formed [2-methyl-3-carbethoxy-5-hydroxybenzofuryl-(6)]-acetoacetic ester (II) and diethyl benzo [1,2-b; 4,5-b']-difuran-3,7-dicarboxylate (III).

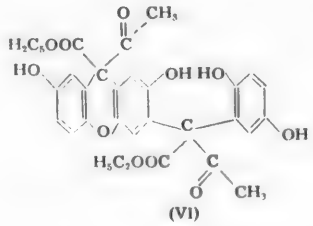


(II)



(III)

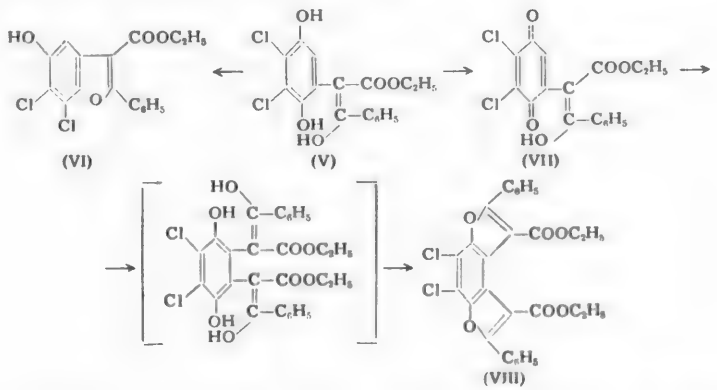
If the reaction is carried out at 38°, only the substituted benzofuran acetoacetic ester (II) is obtained. The latter is obtained without admixture of the benzodifuran derivative (III) when the concentration of zinc chloride in the reaction mixture is decreased. When a solution of the substituted benzofurylacetoacetic ester (II) in alcohol, acetic acid, or other solvents is boiled, it easily changes into the benzodifuran derivative (III). If the reaction is carried out at low temperatures, an increase in the relative concentration of p-benzoquinone in the reaction mixture produces in the reaction product along with the benzofuryl acetoacetic ester (II) a substance with m.p. 206.5-207°, for which the analysis and qualitative reactions indicate the structural formula of a dibenzopyran derivative (IV).



(VI)

In one of our studies [6], as the result of a careful separation of the reaction products from the reaction of 2,3-dichloroquinone with benzoylacetic ester, we isolated one of the hypothetical intermediate compounds, (3,4-dichloro-2,5-dihydroxyphenyl)-benzoylacetic ester (V). In the present paper we show that compound (V) is obtained in good yield if the condensation between 2,3-dichloroquinone and benzoylacetic ester is carried out at temperatures below 60°. The cyclization of the hydroquinone (V) into benzofuran (VI) proceess with definite speed only at 90°. If the temperature of the reaction mixture reaches 100°, the hydroquinone (V) cannot be isolated: it is completely cyclized into the benzofuran derivative (VI).

For confirmation of the reaction mechanism which we have assumed [2,6], (3,4-dichloro-2,5-dihydroxyphenyl)-benzoylacetic ester (V) was oxidized to the corresponding quinone (VII), and the latter was transformed by the action of benzoylacetic ester into the benzodifuran derivative (VIII), which was also isolated as a result of the reaction of 2,3-dichloroquinone with benzoylacetic ester [6].

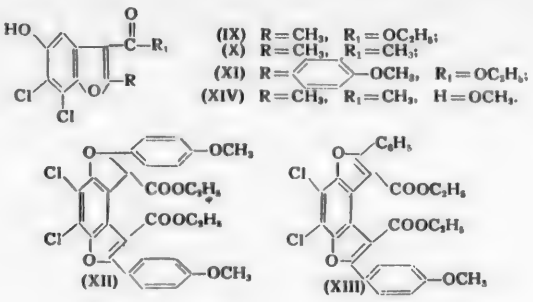


(VI) (V) (VII) (VIII)

On the basis of these studies it is possible to conclude that the one or the other direction of the condensation of quinones with esters of β-ketoacids can easily be determined by a comparison of the yield of benzofuran and benzodifuran derivatives, and depends not only on the quinone concentration in the reaction mixture, but also to a considerable extent on the temperature at which the process is carried out. Besides these factors, the nature of the reagents, which react with the quinone also influence the yields of benzofuran and benzodifuran derivatives.

We carried out under the same conditions the condensation of 2,3-dichloroquinone with acetoacetic ester, acetylacetone, benzoylacetic ester, and p-methoxybenzoylacetic ester, and found that acetoacetic ester and acetylacetone react only to form the substituted benzofurans (IX) and (X). Condensation of 2,3-dichloroquinone with benzoylacetic and p-methoxybenzoylacetic esters leads to the formation of a mixture of derivatives of benzofuran

(VI, XI) and benzodifuran (VIII, XII); the yield of the benzodifuran derivative (XII) in the reaction of 2,3-dichloroquinone with p-methoxybenzoylacetic ester is greater than in the case of the benzoylacetic ester.



In explaining these results it is evidently necessary to consider both the nature of the β-ketoacid ester and the residue which acts as a substituent in the intermediate quinone (VII); the action of these two factors can be contradictory in character. Obviously the direction of the reaction is affected by the different solubilities in the reaction solvent of the intermediate hydroquinones* and differences in their reduction potentials. Since it was not possible in most experiments to isolate the intermediate hydroquinones and so establish their solubilities and reduction potentials, we followed another path: to study the effect of the nature of β-ketoacid ester which reacted with the quinone, we carried out a condensation of 2,3-dichloroquinone benzoylacetic ester (VII) with benzoylacetic ester and p-methoxybenzolacetic ester. We assumed that benzoylacetic and p-methoxybenzoylacetic esters would differ in activity and would react at different rates. Also, since the starting quinone rapidly formed a tar under the reaction conditions, we counted on obtaining the benzodifuran derivatives (VIII), (XIII), with different yields. If the yields of (VIII) and (XIII) differed greatly, then we could hope to increase the yield of benzodifuran derivative (XII) in the condensation of 2,3-dichloroquinone with p-methoxybenzoylacetic ester from the greater activity of the latter compared to benzoylacetic ester. However, the yield of benzodifuran derivatives (VIII) and (XIII) in the reaction of compound (VII) with benzoylacetic and p-methoxybenzoylacetic esters was about the same.

EXPERIMENTAL

Condensation of p-Benzoquinone with Actoacetic Ester

1. The reaction was carried out in an extractor (without a siphon) with a condenser protected by a calcium chloride tube. In the extractor thimble with a volume of 200 ml was placed 21.6 g of p-benzoquinone. The extractor was connected to a three-necked flask (volume 390 ml) fitted with a thermometer. In the flask was placed a solution of 27.3 g of anhydrous zinc chloride in 27 ml of anhydrous ethyl alcohol, 52.3 g of acetoacetic ester, and 120 ml of absolute ether, and the flask was heated on an air bath whose temperature was regulated so that the temperature of the solution in the flask was 44-45°; quinone was added to the flask by extraction during 11.5 hours. When all the quinone had been added the reaction mixture in the flask was kept at the same temperature for 1 hour more. The white crystals which separated were filtered off and washed with ether. Yield 5.2 g, m.p. 183-183.5°. The filtrate, combined with the wash liquid, was washed with water, and then from the solution 1.9 g more of crystals precipitated and had the same melting point. Diethyl 2,6-dimethylbenzo(1,2-b; 4,5-b')-difuran-3,7-dicarboxylate (III) melts, according to the literature, at 184°. A mixed melting point of substance (III) with pure substance (III) gave no depression. The total yield of diethyl 2,6-dimethylbenzo(1,2-b; 4,5-b')difuran-3,7-dicarboxylate (III) was 7.1 g (21.5%).**

The ether solution was dried over magnesium sulfate, the ether was distilled off in a vacuum, and the resulting thick oil remained overnight in a vacuum desiccator over phosphoric anhydride, after which it crystallized. The crystals were filtered and washed with methyl alcohol. Yield 11.2 g, (33.0%), m.p. 125-125.5° (from dichloroethane).

*[3,4-Dichloro-2,5-dihydroxyphenyl]-benzoylacetic ester (V) for example, because of its poor solubility in the reaction solution, precipitates out.

**In all the experiments the yields are calculated on the starting quinone.

Found %: C 62.02, 61.78; H 5.90, 5.73. $C_{18}H_{20}O_7$. Calculated %: C 62.06; H 5.79.

The resulting white, crystalline substance was easily soluble in dichloroethane and dioxane, somewhat less so in ether. With heat it dissolved in alcohol, acetic acid, and all solvents which contained water; it was easily changed into the diethyl 2,6-dimethylbenzo(1,2-b; 4,5-b')difuran-3,7-dicarboxylate (III). With p-benzoquinone it did not form a quinhydrone, but with solutions of ferric chloride it gave a colored solution. From the analytical data and its chemical properties, the substance is [2-methyl-3-carbethoxy-5-hydroxybenzofuryl-(6)]acetoacetic ester (II).

2. For the reaction we took 21.6 g of p-benzoquinone, 52.3 g of acetoacetic ester, a solution of 13.6 g of anhydrous zinc chloride in 14 ml of anhydrous ethyl alcohol, and 120 ml of absolute ether. The reaction was carried out in the same way as in experiment 1, but the alcohol solution of zinc chloride was gradually added to the three necked flask from a dropping funnel. Before the reaction began, about 1/4 of the whole zinc chloride solution was added, and then it was added at the rate of 20-30 drops per hour. After 8 hours from the beginning of the reaction there was evident formation of quinhydrone, after which half the remaining zinc chloride solution was added, and over another hour, the rest. The addition of the zinc chloride solution took 9 hours. The reaction was run at 43-45°. p-Benzoquinone was extracted into the flask for 13.5 hours. After this the reaction mixture was kept at the same temperature for a further 1.5 hours. The resulting ether solution was treated as in experiment 1. Diethyl 2,6-dimethyl-benzo(1,2-b; 4,5-b')difuran-3,7-dicarboxylate (III) was not obtained. The yield of[2-methyl-3-carbethoxy-5-hydroxybenzofuryl-(6)]acetoacetic ester (II) was 10.5 g (30.2%), m.p. 125-126°. A mixed melting point with ester(II)obtained in experiment 1 gave no depression.

3. For the experiment we took 10.8 g of p-benzoquinone, 15.4 g of acetoacetic ester, a solution of 13.6 g of anhydrous zinc chloride in 14 ml of anhydrous ethyl alcohol, and 120 ml of absolute ether. Reaction was carried out as in experiment 1. p-Benzoquinone was extracted for 12.5 hours at 38°. After the addition of all the quinone the reaction mixture was kept at the same temperature for 1.5 more hours. The resulting ether solution was treated as in experiment 1. The yield of [2-methyl-3-carbethoxy-5-hydroxybenzofuryl-(6)]acetoacetic ester (II) was 6.3 g (36.3%), m.p. 125°. A mixed melting point with ester (II) from experiment 1 gave no depression.

4. For the experiment we took 10.8 g of p-benzoquinone, 15.4 g of acetoacetic ester, a solution of 13.6 g of anhydrous zinc chloride in 14 ml of anhydrous ethyl alcohol, and 120 ml of anhydrous ether. The reaction was run as in experiment 1, but at 40-41°. p-Benzoquinone was extracted for 11 hours. After addition of all the p-benzoquinone, the reaction mixture was kept at the same temperature for a further 1.5 hours. The resulting solution was treated as in experiment 1. After the solution was dried over magnesium sulfate, white crystals precipitated. They were filtered off, washed with ether, freed by water from magnesium sulfate, and dried. Yield 2.9 g (20.6%), m.p. 206.5-207°.

Found %: C 63.65, 63.58; H 4.73, 4.72. $C_{30}H_{28}O_{11}$. Calculated %: C 63.86; H 4.99.

The compound was easily soluble in dichloroethane, benzene, methyl and ethyl alcohols; poorly soluble in benzine. With p-benzoquinone it formed with heat a quinhydrone, and gave a color reaction with ferric chloride. From the analytical data and chemical properties it was a dibenzopyran derivative (IV).

From the ether solution we obtained 2.5 g (14.4%) of[2-methyl-3-carbethoxy-5-hydroxybenzofuryl-(6)]acetoacetic ester (II) with m.p. 124.5-125°. A mixed melting poin' with(II)obtained in experiment 1 gave no depression.

Condensation of 2,3-Dichloroquinone with Acetoacetic Ester

1. The reaction was carried out in a three-necked flask connected with a stirrer, thermometer, and reflux condenser protected by a calcium chloride tube. In the flask we placed a solution of 6.8 g of anhydrous zinc chloride in 7 ml of anhydrous ethyl alcohol and 19.5 g of acetoacetic ester; the solution was heated to 100° on the water bath and 8.9 g of 2,3-dichloroquinone was quickly added to it. The reaction mixture was heated for 40 minutes with stirring on the water bath. The resulting crystals of 2-methyl-3-carbethoxy-5-hydroxy-6,7-dichlorobenzofuran (IX) were washed with water to remove zinc chloride, then with methyl alcohol, and were dried. Yield 7.3 g (53.5%), m.p. 196-197°. After 2 recrystallizations from methyl alcohol, the m.p. was 201° [7].

2. For the experiment we took 8.9 g of 2,3-dichloroquinone, a solution of 6.8 g of anhydrous zinc chloride in 7 ml of anhydrous ethyl alcohol, and 7.2 g of acetoacetic ester. Reaction was carried out as in the previous experiment. The acetoacetic ester was added to the alcoholic zinc chloride solution and the 2,3-dichloroquinone

was added to the resulting solution over 20 minutes at 85-90°. The reaction mixture was kept at the same temperature for 30 minutes more. The resulting crystals of 2-methyl-3-carbethoxy-5-hydroxy-6,7-dichlorobenzofuran (IX) were washed with water and methyl alcohol. Yield 4.8 g (35.2%), m. p. 195-196°. After 2 recrystallizations from methyl alcohol the m.p. was 200-201°; according to the literature it is 202.5° [7].

Condensation of 2,3-Dichloroquinone with Acetylacetone

For the experiment we took 8.9 g of 2,3-dichloroquinone, a solution of 6.8 g of anhydrous zinc chloride in 7 ml of anhydrous ethyl alcohol, and 5.2 g of acetylacetone. The reaction was carried out in a manner analogous to the condensation of 2,3-dichloroquinone with acetoacetic ester. The resulting crystals were washed with water, methyl alcohol, and ether. Yield of 2-methyl-3-acetyl-5-hydroxy-6,7-dichlorobenzofuran (X) 7.4 g (57.2%). They melted with decomposition at 260.5° (from dioxane). White crystals, easily soluble in dioxane, toluene, and dichloroethane.

Found %: C 50.75, 50.70; H 3.11, 3.16. $C_{11}H_8O_3Cl_2$. Calculated %: C 50.99; H 3.11.

Preparation of 2-methyl-3-acetyl-5-methoxy-6,7-dichlorobenzofuran (XIV). To 2.8 g of 2-methyl-3-acetyl-5-hydroxy-6,7-dichlorobenzofuran (X) was added 70 ml of dioxane and 11 ml of 2 N sodium hydroxide solution. The resulting phenolate solution was treated in small portions with 9.5 ml of dimethyl sulfate. The reaction mixture was shaken on a rocker for 2 hours. The 2-methyl-3-acetyl-5-methoxy-6,7-dichlorobenzofuran (XIV) which was formed dissolved almost completely. The solution was diluted with double its amount of water and the precipitate was filtered. Yield 2.8 g (95.0%), m.p. 188-189° (from dioxane). White needles, easily soluble in dichloroethane and dioxane, less so in methyl alcohol.

Found %: C 52.79, 52.98; H 3.81; 3.84. $C_{12}H_{10}O_3Cl_2$. Calculated %: C 52.77; H 3.69.

Condensation of 2,3-Dichloroquinone with Benzoylacetic Ester

1. For the experiment we took 7.5 g of 2,3-dichloroquinone, a solution of 5.7 g of anhydrous zinc chloride in 6 ml of anhydrous ethyl alcohol, and 8.8 g of benzoylacetic ester. The reaction was carried out analogously to the condensation of 2,3-dichloroquinone with acetoacetic ester at 100° (expt. 1). The resulting crystals were washed with water and methyl alcohol. Yield of 2-phenyl-3-carbethoxy-5-hydroxy-6,7-dichlorobenzofuran (VI) 8.0 g (54.5%), m.p. 184-186°. According to the literature [7], m.p. 185.5-186°. The benzodifuran derivative (VIII) was not found in this case.

2. For the experiment we took 20 g of 2,3-dichloroquinone, a solution of 15.4 g of anhydrous zinc chloride in 16 ml of anhydrous ethyl alcohol, 26.5 g of benzoylacetic ester, and 55 ml of absolute ether. The reaction was run under the conditions for the condensation of p-benzoquinone with acetoacetic ester (expt. 1), but the 2,3-dichloroquinone was extracted 2.5 hours in the reaction vessel at 55-61°. After addition of all the quinone, the reaction mixture was heated for 2 hours more. The white crystals which precipitated were filtered, washed with ether and water, and dried. Yield 8.9 g (45.5%), m.p. 164.5-165° (from dichloroethane).

Found %: C 55.22, 55.17; H 3.85, 3.82. $C_{17}H_{14}O_5Cl_2$. Calculated %: C 55.34; H 3.80.

The resulting substance was easily soluble in dichloroethane, acetic acid, and methyl and ethyl alcohols. It formed a quinhydrone with p-benzoquinone and gave a color reaction with ferric chloride. From the analytical results and the chemical properties it was (3,4-dichloro-2,5-dihydroxyphenyl)-benzoylacetic ester (V).

3. For the experiment we took 8.9 g of 2,3-dichloroquinone, a solution of 6.8 g of anhydrous zinc chloride in 7 ml of anhydrous ethyl alcohol, and 10.6 g of benzoylacetic ester. The reaction was run analogously to the condensation of 2,3-dichloroquinone with acetoacetic ester, but at 55-63°. The precipitating crystals were washed with water and methyl alcohol. Yield 10.6 g, m.p. 160-162°. The substance was dissolved in 265 ml of ethyl alcohol. When the solution cooled, crystals precipitated (0.1 g, 0.77%) with m.p. 229° which corresponded to the m.p. of diethyl 7,8-dichloro-2,5-diphenylbenzo(1,2-b; 5,6-b')-difuran-3,4-dicarboxylate (VIII) [6]. (3,4-Dichloro-2,5-dihydroxyphenyl)-benzoylacetic ester (V) separated when the alcohol solution was evaporated. The yield of ester(V)was 10.5 g (57.0%), m.p. 164-164.5° (after recrystallization from dichloroethane).

Oxidation of (3,4-dichloro-2,5-dihydroxyphenyl)-benzoylacetic ester (V) to the quinone (VII). Silver oxide, precipitated from a solution of 10 g of silver nitrate in water by 20% sodium hydroxide, was washed on the filter, 12 times with water, 6 times with acetone, and 6 times with absolute ether and placed in a beaker under a layer

of absolute ether. 5.2 g of (3,4-dichloro-2,5-dihydroxyphenyl)-benzoylacetic ester (V) was dissolved in 410 ml of absolute ether and to the resulting solution was added 20 g of anhydrous magnesium sulfate and the prepared silver oxide. The reaction mixture was shaken for 10 minutes. The solution was separated from the precipitate and the ether distilled from it in a vacuum at room temperature. The resulting yellow crystals of the quinone (VII) were washed with a little ether. Yield 3.1 g (58.4%), m.p. 102-103°. After recrystallization from ether, m. p. 103.5-104°.

Found %: C 55.92, 55.71; H 3.39, 3.51. $C_{17}H_{12}O_5Cl_2$. Calculated %: C 55.60; H 3.29.

The resulting substance gave a quinhydrone with hydroquinone and a color reaction with ferric chloride.

Condensation of the Quinone (VII) with Benzoylacetic Ester

In a test tube closed by a glass tube with a Bunsen valve was placed a solution of 0.4 g of anhydrous zinc chloride in 0.4 g of anhydrous ethyl alcohol, 0.67 g of benzoyl acetic ester, and 1 g of quinone (VII). The reaction mixture was heated for 1 hour on a boiling water bath. The resulting crystals were washed free of zinc chloride with water and then with methyl alcohol and ether. Yield 0.5 g (35.4%). After recrystallization from a mixture of dioxane and ethyl alcohol, m.p. 227°. A mixed melting point with pure diethyl 7,8-dichloro-2,5-diphenyl-benzo-(1,2-b; 5,6-b')-difuran-3,4-dicarboxylate (VIII) [6] gave no depression.

Condensation of 2,3-Dichloroquinone with p-Methoxybenzoylacetic Ester

1. For the experiment we took 7.7 g of 2,3-dichloroquinone, a solution of 5.9 g of anhydrous zinc chloride, and 6 ml of anhydrous ethyl alcohol and 10.6 g of p-methoxybenzoylacetic ester [8]. The reaction was carried out under the conditions of condensation of 2,3-dichloroquinone with acetoacetic ester at 100° (experiment 1). The resulting crystals were washed with water and methyl alcohol, placed in an extractor thimble, and extracted with 3700 ml of ether. After removal of the ether we obtained 9.6 g (58%) of a substance with m.p. 175-176°. The pure substance melted at 183.5-184° (from ethyl alcohol).

Found %: C 56.97, 57.18; H 3.97, 3.81. $C_{18}H_{14}O_5Cl_2$. Calculated %: C 56.70; H 3.70.

According to the analytical data, this substance is 2-(p-methoxyphenyl)-3-carbethoxy-5-hydroxy-6,7-dichlorobenzofuran (XI). It was easily soluble in dichloroethane, dioxane, and ethyl alcohol.

In the residue after extraction was found 1 g (7.9%) of a white substance with m.p. 248.5-249°. The pure substance melted at 257.75° (from aqueous dioxane).

Found %: C 62.10, 62.03; H 4.21, 4.11. $C_{30}H_{24}O_8Cl_2$. Calculated %: C 61.76; H 4.13.

According to the analytical data this substance is diethyl 7,8-dichloro-2,5-di-(p-methoxyphenyl)-benzo (1,2-b; 5,6-b')-difuran-3,4-dicarboxylate (XII).

2. For the experiment we took 8.9 g of 2,3-dichloroquinone, a solution of 6.8 g of anhydrous zinc chloride in 7 ml of anhydrous ethyl alcohol, and 12.2 g of p-methoxybenzoylacetic ester. The reaction was carried out under the conditions of the condensation of 2,3-dichloroquinone with benzoylacetic ester at 85-90° [6]. The resulting crystals were washed with water and methyl alcohol, and extracted with 420 ml of ether. From the ether solution we obtained 6.8 g (35.7%) of 2-(p-methoxyphenyl)-3-carbethoxy-5-hydroxy-6,7-dichlorobenzofuran (XI), with m.p. 172.5-175°, m.p. 180° from dichloroethane. A test of the mixture with the preparation of (XI) obtained in the previous experiment gave no depression of the melting point.

After extraction there remained 2.6 g (17.8%) of diethyl 2,5-di(p-methoxyphenyl)-benzo-(1,2-b; 5,6-b')-difuran-3,4-dicarboxylate (XII) with m.p. 255-256°. A mixed melting point with preparation (XII) from the previous experiment gave no depression.

Condensation of Quinone (VII) with p-Methoxybenzoylacetic Ester

For the experiment we took 1 g of quinone (VII), a solution of 0.75 g of anhydrous zinc chloride in 0.8 ml of anhydrous ethyl alcohol, and 1.3 g of p-methoxybenzoylacetic ester. The reaction was carried out as in the condensation of quinone (VII) with benzoylacetic ester. The yield of diethyl 7,8-dichloro-2-phenyl-5-(p-methoxyphenyl)-benzo(1,2-b; 5,6-b')-difuran-3,4-dicarboxylate (XIII) was 0.5 g (33.5%), m.p. 216.5°. The pure substance melted at 218.5-219° (from dioxane).

Found %: C 63.25, 63.36; H 4.12, 4.25. $C_{19}H_{22}O_7Cl_2$. Calculated %: C 62.94; H 4.01.

SUMMARY

In examples of the condensation of p-benzoquinone and 2,3-dichloroquinone with acetoacetic ester and its analogs we have shown that the result of this reaction depends on the concentration of quinone in the reaction mixture and also on the reaction temperature and the nature of the reagents which react with the quinone.

The course of the reactions (isolation of intermediate products and separation of the different steps in the process) confirms our earlier assumption as to the mechanism of the reaction.

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THE REACTION OF KETENE WITH NITROGEN-CONTAINING BASES

VII. CHLOROACETYLATION OF PRIMARY AMINES

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The exceptional mobility of the chlorine atom in compounds of the type $RNHCOCH_2Cl$, $RNHCOCHCl_2$, and $RNHCOCCl_3$ has opened wide synthetic possibilities which were used in different fields of organic chemistry. Thus, for example, Stollé [1] and others have shown that chloroacetanilide is a good starting point for the synthesis of indigo dyes. Recently, α-chloroacetyl derivatives of amines have been widely used for obtaining physiologically active substances [2]. On the other hand, chloroacetanilide is itself interesting for medicine [3], since it is used for local anesthesia and as a substance to counteract the initiation of tuberculosis, angina, etc. This compound is also a rather strong insectofungicide.

At the present time, several methods are known for the synthesis of chloroacetanilide [4-9]. However, a distinguishing characteristic of these methods is the number of steps, the need for rare reagents, and the possibility of side reactions. From this point of view, the reaction of ketene with halogen substituted acids is promising; it proceeds through the formation of mixed anhydrides. The literature contains evidence of the chloroacetylating action of these anhydrides [10], but unfortunately, does not give a method of synthesis. Therefore we have worked out the synthetic part of the reaction of chloroacetylation from the beginning. The positive advantages of our method make it the simplest for obtaining chloroacetanilides.

EXPERIMENTAL

To 10 g of monochloroacetic acid (m.p. 61°) placed in a three-necked flask fitted with a mechanical stirrer, reflux condenser, and glass inlet, was added ketene over 15-20 minutes.* After vacuum distillation we obtained a mixed anhydride of acetic and chloroacetic acids with b.p. 118-120° (110 mm) (12.7 g), which was cooled with a mixture of snow and salt and added with stirring to 7 g of aniline. The resulting precipitate remained for 10-20 minutes in the reaction vessel, then was recrystallized from water with active charcoal; m.p. 134°, yield 78%.

This operation could be carried out with the same yield in one step, without separating the pure anhydride. In this case, after passing ketene into the chloroacetic acid, the resulting liquid was added to the calculated amount of amine without cooling; then 1-2 ml of water was added. Immediately a voluminous precipitate of chloroacetyl derivative formed and was recrystallized from water.

The results of the work are given in the Table.

Formula of chloroacetyl derivatives of the amine	Yield (in %)	Melting point	% Cl	
			Found	Calculated
$C_6H_5NHCOCH_2Cl$	78	134°	20.53	20.93
o-$CH_3C_6H_4NHCOCH_2Cl$	63	110—111	19.22	19.30
m-$CH_3C_6H_4NHCOCH_2Cl$	72	141	19.15	19.30
p-$CH_3C_6H_4NHCOCH_2Cl$	67	161	20.24	19.30
p-J-$C_6H_4NHCOCH_2Cl$	58	189	12.07	11.99
o-$CH_3OC_6H_4NHCOCH_2Cl$	61	49	17.52*	17.60
p-$CH_3OC_6H_4NHCOCH_2Cl$	66	121.5	17.73*	17.60

*The chlorine content was determined by the adsorption method.

*Ketene was obtained by the pyrolysis of acetone at 700° (50 ml of acetone used).

SUMMARY

We have given a new method for preparing chloroacetyl derivatives of amines by the action of chloroacetic acid and ketene on amines.

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STUDIES OF ORGANIC SULFUR COMPOUNDS

I. THE SYNTHESIS OF ALKANESULFONYL FLUORIDES AND THEIR HALOGEN DERIVATIVES

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The class of aliphatic sulfonyl fluorides has been very little studied. The unsaturated sulfonyl fluorides have been studied still less and only vinylsulfonyl fluoride has been described [1]. Among the aliphatic sulfonyl fluorides which have been obtained there are substances with useful properties. Thus, methanesulfonyl fluoride is an effective insecticide [2], and the vinylsulfonyl fluoride which was mentioned copolymerizes with acrylonitrile to give a resin with high heat stability and plasticity [1].

In the present work we have carried out the synthesis of some alkanesulfonyl fluorides and their halogen derivatives (a number of which have not been described in the literature), in accordance with the general scheme:

$$RSO_2Cl \xrightarrow[HgF_2]{KF,ZnF_2} RSO_2F,$$

where: R=CH_3, n-C_3H_7, iso-C_3H_7, CH_2Cl, CH_2I, CH_2FCH_2, CH_3CHCl, CH_2ClCH_2, CH_2BrCH_2, $CHCl_2CH_2$, $O_2NCH_2CH_2$.

Davis and Dick showed that the action of an aqueous solution of potassium fluoride on α-chloroethane-, cyclohexane-, and benzenesulfonylchloride gave the corresponding sulfonyl fluorides [3]. They carried out the reaction by heating the reacting substances with stirring; the precipitate of potassium chloride was dissolved in water; after ether extraction the dried extract was distilled. However, as these authors themselves showed, this method was not suitable for the synthesis of the first member of the series, methanesulfonyl fluoride, for the preparation of which they used another process (the action of zinc fluoride on methanesulfonyl chloride in a platinum vessel with heating).

We have found conditions by which methanesulfonyl fluoride can be prepared in good yield from methanesulfonyl chloride by the action of a saturated solution of potassium fluoride [4]. For this purpose the reacting substances are heated to boiling in a Favorskii flask and the methanesulfonyl fluoride which forms is distilled directly with steam. The methanesulfonyl fluoride which separates from the water layer contains almost no admixtures and comes over completely in the narrow temperature range (yield 65%).

In the same way we synthesized the undescribed n- and isopropanesulfonyl fluorides, and also iodomethanesulfonyl fluoride. Our experiments on obtaining this substance by the method of Davis and Dick showed that it could not be obtained in this way, and the first two substances formed along with contaminating impurities which were difficult to separate.

Thus, our method is simple and suitable for obtaining methane-, iodomethane-, n-propane- and isopropanesulfonyl fluorides.

We should say that the transformation of halogen substituted alkanesulfonyl chlorides (especially those substituted in the β-position) occurs with a sharply decreased yield of the corresponding sulfonyl fluorides because of competing processes [5] which in some cases become predominant. For example, β,β-dichloroethanesulfonyl fluoride cannot be obtained by the action of potassium fluoride in water solution, and this substance was obtained

by the action of zinc fluoride on the starting sulfonyl chloride.* β-Chloroethanesulfonyl fluoride was isolated under the conditions of our reaction, but the yield was very low.

It is worthy of remark that the action of potassium fluoride, ammonium fluoride or zinc fluoride fails to convert trichloromethanesulfonyl chloride into trichloromethanesulfonyl fluoride; either the reaction does not occur at all, or there is deep destruction of the molecule with formation of carbon tetrachloride, hexachloroethane, and sulfur dioxide.

The increment of atomic refraction of fluorine in the sulfonyl fluorides which we have synthesized differs from the figure accepted for this value (0.997-1.08). In most cases the value for the atomic refraction of fluorine in the sulfonyl fluorides is close to 1.61, although we have found considerable variation on one side or the other depending on the structure and characteristics of the substituents in the hydrocarbon radical. Such a high value for the atomic refraction of fluorine has also been observed in other compounds which contain fluorine [6].

EXPERIMENTAL

Methanesulfonyl fluoride (I). We placed in a Favorskii flask 30 g of methanesulfonyl chloride and 90.9 g of a 70% solution of potassium fluoride. The mixture was heated on a wire gauze until distillation of a two layer liquid stopped (89-90°). The distillate was separated, the organic layer was dried over calcium chloride, and distilled. Yield of(I)18 g (65%).

B.p. 124-124.2°, $n^{20}D$ 1.3568, d^{20}_4 1.3470, MR_D 15.94, AR_F 1.61.
Literature data for (I): b.p. 124.2° (754 mm), $n^{20}D$ 1.3596 [3].

n-Propanesulfonyl fluoride (II). n-Propane- and isopropanesulfonyl chlorides were separated by fractional distillation from the product of sulfochlorination of propane. 16.8 g of n-propanesulfonyl chloride (b.p. 76-78° at 13 mm, $n^{20}D$ 1.4536) was treated with 24 g of saturated potassium fluoride solution and the 90-94° fraction was collected. The organic layer after drying over calcium chloride came over completely in the range 148-150° (749 mm).

$n^{20}D$ 1.3865, d^{20}_4 1.2003, MR_D 24.71; calcd. 24.56; AR_F 1.14.
Found %: F 15.2, 15.4. $C_3H_7O_2SF$. Calculated %: F 15.07.

Isopropanesulfonyl fluoride (III). From 50 g of isopropanesulfonyl chloride (b.p. 71.0-73° at 13 mm, $n^{20}D$ 1.4520) and 76 g of 70% potassium fluoride solution we obtained(III)(not containing chloride).

B.p. 144-146° (751 mm), $n^{20}D$ 1.3895, d^{20}_4 1.1600, MR_D 25.74; calcd. 24.56.
Found %: F 15.5, 15.6. $C_3H_7O_2SF$. Calculated %: F 15.07.

Chloromethanesulfonyl fluoride (IV). As the starting substance we used chloromethanesulfonyl chloride, obtained by oxidative chlorination of 1,3,5-trithiane, which was formed by the action of hydrogen sulfide on paraform in a hydrochloric acid medium [7]. 151 g of chloromethanesulfonyl chloride (b.p. 172-174°) was treated with 300 g of a solution of potassium chloride under the conditions of Davis and Dick. We obtained 59 g of(IV); yield 43.7%.**

B.p. 130-132°, $n^{20}D$ 1.4123, d^{20}_4 1.5980, MR_D 20.58; calcd. 20.64.
Literature data for (VI) [8]: b.p. 131.5-132°.

Iodomethanesulfonyl fluoride (V). 50 g of skiodan was treated with 44 g of phosphorus pentachloride with shaking. When the reaction was ended (the mixture no longer warmed spontaneously), the content of the flask was poured onto ice and the oil which precipitated was extracted with benzene; the extract was dried with calcium chloride and distilled. We obtained 46 g (91.2%) of iodomethanesulfonyl chloride.

B.p. 82-83° (2 mm), b.p. 93° (5 mm), $n^{20}D$ 1.4840, d^{20}_4 2.4465, MR_D 32.91; calc. 33.36.

21.5 g of iodomethanesulfonyl chloride was treated with 45 g of a saturated solution of potassium fluoride and substance (V) was obtained.

*β,β-Dichloroethanesulfonyl chloride, described by Iakubovich and Zinov'ev [13], can be prepared, as Kochetkov showed, by combination of sulfuryl chloride and vinyl chloride in the presence of aluminum chloride [14].
**Under the conditions described for(I),the yield of chloromethanesulfonyl fluoride fell to 29.4%.

B.p. 64-64.5° (5 mm), $n^{20}D$ 1.5090, d^{20}_4 2.3236; MR_D 28.76; calcd. 28.12.
Found %: C 5.93, 5.98; H 1.26, 1.02; S 14.11 , 13.74; F 7.99, 8.27. CH_2O_2SFI. Calculated %: C 6.57; H 0.89; S 14.9; F 8.45.

β-Fluoroethanesulfonyl fluoride (VI). The starting β-fluoroethanesulfonyl chloride was obtained in 57% yield and identified by its constants [9]. From 15.5 g of β-fluoroethanesulfonyl chloride (b.p. 82-85° at 13 mm, $n^{20}D$ 1.4570) and 40 g of potassium fluoride we obtained 4.8 g of a substance with b.p. 118-120° at 757 mm ($n^{20}D$ 1.3845 [5]) and substance (VI).

B.p. 164-166° (757 mm), $n^{20}D$ 1.4150, d^{20}_4 1.4157, MR_D 23.06.
Found %: F 30.4, 30.6. $C_2H_4O_2SF_2$. Calculated %: F 29.09.

α-Chloroethanesulfonyl fluoride (VII). 16 g of α-chloroethanesulfonyl chloride was reacted with 36 g of a solution of potassium fluoride under the conditions of Davis and Dick. We obtained 1.5 g (10.5) of substance (VII).

B.p. 138.0-139° (760 mm), $n^{20}D$ 1.4080, d^{20}_4 1.4420, MR_D 25.05; calcd. 25.01.
Literature data for (VII) [3]: b.p. 138-139° (760 mm), $n^{20}D$ 1.4070.

β-Chloroethanesulfonyl fluoride (VIII). β-Chloroethanesulfonyl chloride was obtained according to the data of [10]. To 17.9 g of β-chloroethanesulfonyl chloride (b.p. 70-71° at 5 mm, $n^{20}D$ 1.4910) was added 45 ml of a saturated solution of potassium fluoride and the reaction was carried out as described for (I). The organic layer, dried over calcium chloride, was distilled and fractions were separated: 1st, 118-120° (747 mm), $n^{20}D$ 1.3850, 10.9 g; 2nd, 164-166° (757 mm), $n^{20}D$ 1.4258, 2.3 g; 3rd, 170-172° (758 mm), $n^{20}D$ 1.4337, 1.7 g. The 1st and 2nd fractions were not further studied; the 3rd was substance (VII).

B.p. 170-172° (758 mm), $n^{20}D$ 1.4337, d^{20}_4 1.5007, MR_D 25.41; calcd. 25.01.
Found %: Cl 24.6, 24.8; F 12.45, 12.74. $C_2H_4O_2SFCl$. Calculated %: Cl 24.21; F 12.95.

β-Bromoethanesulfonyl fluoride (IX). β-Bromoethanesulfonyl chloride was obtained by the reaction of 1,2-dibromoethane and sodium sulfite with later treatment of the thus formed β-bromoethanesulfonate by phosphorus pentachloride [11]. Substance (IX) was synthesized from 8 g of a saturated potassium fluoride solution and 3 g of β-bromoethanesulfonyl chloride.

B.p. 77° (5 mm), $n^{20}D$ 1.4870.
Found %: F 10.4, 10.4. $C_2H_4O_2SFBr$. Calculated %: F 9.95.

β,β-Dichloroethanesulfonyl fluoride (X). 20 g of β,β-dichloroethanesulfonyl chloride was heated 18 hours in a platinum flask with 20 g of zinc fluoride* to 100-160°; 4 more g of zinc fluoride was added and heating was continued for 6 hours to 165-170°. We obtained 4.5 g (25%) of substance (X).

B.p. 62-64° (5 mm), b.p. 74-76° (25 mm), $n^{20}D$ 1.4527, d^{20}_4 1.6169, MR_D 30.24; calcd. 29.88.
Found %: F 10.17, 10.20. $C_2H_3O_2SFCl_2$. Calculated %: F 10.49.

β-Nitroethanesulfonyl fluoride (XI). In a boiling solution of 48 g of potassium hydroxide in 68 g of water was passed sulfur dioxide to a weakly alkaline reaction (pH 9). The resulting solution of potassium bisulfite at 30° was treated dropwise with 52 g of β-nitroethylacetate. We obtained 45 g of the potassium salt of β-nitroethanesulfonic acid (yield 59%) which after careful drying was mixed with 68.5 g of phosphorus oxychloride and 62 g of phosphorus trichloride and was chlorinated with gaseous chlorine for 2 hours. The reaction mass was then filtered, the precipitate washed with phosphorus oxychloride, and the filtrate was distilled. After the phosphorus oxychloride was distilled off the residue was decomposed with water and the oil which precipitated was extracted with benzene. After the benzene had been distilled off the residue of β-nitroethanesulfonyl chloride** (1.6 g) was treated in the cold with mercuric fluoride (in portions). Reaction took place violently, with strong heating. The reaction mixture was extracted three times with ether, the ether extract was washed with 10% hydrochloric acid, and with water, dried over sodium sulfate, and distilled. We collected the fraction (XI) with b.p. 80-82° (2 mm), $n^{20}D$ 1.4352.

Found %: F 12.2, 11.9. $C_2H_4O_4NFS$. Calculated %: F 12.0.

*The action of an aqueous solution of potassium fluoride did not give a pure preparation of substance (X).

**The preparation of β-nitroethanesulfonyl chloride was carried out by the method of Gold and Druner [12].

Action of zinc, antimony, and potassium fluorides on trichloromethanesulfonyl chloride. Equimolecular amounts of trichloromethanesulfonyl chloride and zinc fluoride were carefully heated in a platinum flask. The liquid which passed over completely below −10° was collected in a trap cooled to −78° and absorbed by a solution of sodium hydroxide. This substance was identified as sulfur dioxide. From the reaction mass was distilled a fraction (b.p. 74-78°, n_D^{20} 1.4614, d_4^{20} 1.593) which was carbon tetrachloride. At 150° white crystals came over (m.p. 172-175°) which had a characteristic odor, were poorly soluble in ether, and after two sublimations melted at 182-184°; they were hexachloroethane. The action of antimony trichloride on trichloromethanesulfonyl chloride led to analogous products. A solution of potassium fluoride under the conditions of Davis and Dick had no action on trichloromethanesulfonyl chloride.

SUMMARY

1. We have synthesized n-propane-, isopropane-, iodomethane-, β-fluoroethane-, β-chloroethane-, β-bromoethane-, β-nitroethane-, and β,β-dichloroethanesulfonyl fluorides, which have not been described in the literature.

2. We have shown that heating methane-, n-propane-, isopropane-, and iodomethanesulfonyl chlorides with a saturated solution of potassium fluoride with continuous steam distillation of the resulting sulfonyl fluorides is a satisfactory preparative method for the synthesis of these substances.

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STUDIES OF ORGANIC SULFUR COMPOUNDS

II. THE SYNTHESIS OF ALKENESULFONYL FLUORIDES AND THEIR HALOGEN DERIVATIVES

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In the previous communication we showed that potassium fluoride in water solution acted on some alkanesulfonyl chlorides with continuous steam distillation of the reaction products to give a satisfactory preparative method for the synthesis of some alkane- and haloalkanesulfonyl fluorides [1].

A study of the reaction of potassium fluoride with halogen substituted ethane sulfonyl chlorides showed that along with the replacement of chlorine by fluorine there occurred a process of dehydrohalogenation, as a result of which unsaturated sulfonylfluorides were formed.

$$\underset{\underset{X}{|}}{CH_2}-CH_2SO_2Cl \xrightarrow{2KF} CH_2=CH-SO_2F,$$

(X = F, Cl, Br.)

$$\begin{matrix} Cl \\ Cl \end{matrix}\!\!>\!CH-CH_2SO_2Cl \xrightarrow{2KF} ClCH=CH-SO_2F$$

The ability of alkali fluorides to combine with hydrogen halides and thus give double salts has long been known. Earlier [2] the ability of potassium fluoride to split hydrogen chloride from acid chlorides and alkyl halides was demonstrated.

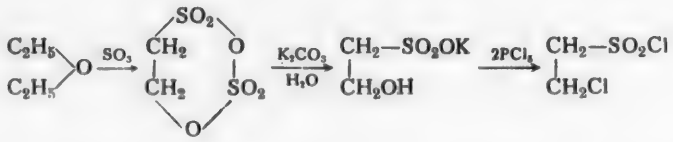
The property of potassium fluoride of splitting hydrogen halides from two adjacent hydrocarbon atoms permitted us to carry out a direct transformation from a halogen derivative of an alkanesulfonyl chloride to a sulfonyl fluoride of the unsaturated series in one step and with good yield. Up to now, only one example of this series has been described, vinylsulfonyl fluoride [3].

This reaction has been used for the synthesis of the unsaturated aliphatic sulfonyl fluorides and their halogen derivatives. The constants of the resulting substances are given in Table 1.

TABLE 1

Substance	Boiling point	Pressure (mm)	n_D^{20}	d_4^{20}	MR_D found	MR_D calc.	Melting point
$CH_2=CH-SO_2F$	118—120°	747	1.3850	1.3329	19.37	19.58	—
$ClCH=CH-SO_2F$ (low boiling)	42.7—43.1	25	1.4170	1.5384	24.40	24.44	—45.8°
$ClCH=CH-SO_2F$ (high boiling)	45.0	25	1.4321	1.5247	24.58	24.44	—22.2
$ClCH=CHSO_2Cl$	50—52	3	1.5043	1.5858	30.09	29.69	—

The starting substances for the synthesis of sulfonyl fluorides of the unsaturated type and their halogen derivatives, as was said above, were the haloalkanesulfonyl chlorides. Thus, β-chloroethanesulfonyl chloride, for whose synthesis no satisfactory method is described in the literature, was obtained by the method of Hübner [4].



It should be said that when β-chloroethanesulfonyl chloride was obtained by this method, the yields were low. The use of an improved method did not affect the yield [5].

A very satisfactory process for preparing β,β-dichloroethanesulfonyl chloride is that described by Kochetkov by direct combination of sulfuryl chloride with vinyl chloride in the presence of anhydrous aluminum chloride [6].

The resulting β-chloro- and β,β-dichloroethanesulfonyl chlorides were transformed into vinyl- and β-chlorovinylsulfonyl chlorides by the action of potassium fluoride. An analogous procedure was applied to the action of potassium fluoride on β-fluoro- and β-bromoethanesulfonyl chlorides, whose preparation was described earlier [1].

We isolated two fractions with similar boiling points from β-chlorovinylsulfonyl fluoride, which were stereoisomers (Table 1). In many cases in the ethylene series of hydrocarbons the isomers with the lower values for boiling point and constants have the trans configuration, and the isomers with the higher boiling points and higher constants have the cis configuration. However, the reverse relationship is often found. Neither these nor any other regularities exist between boiling points and other basic constants for the isolated fractions of β-chlorovinylsulfonyl fluorides.

Examples are described in the literature of ethylene hydrocarbons (with established or unknown configurations), the regularities of whose boiling points and also the tendency for the constants to change is similar to those found for the β-chlorovinyl sulfonyl fluoride isomers: for the low boiling isomer the refractive index is lower and the specific gravity is higher. Table 2 illustrates these values.

Thus, substances with freezing points of −45.0 and −22.2° (Table 1) on the basis of elementary analysis, constants, and molecular refraction can be ascribed the structures of cis and trans β-chlorovinylsulfonyl fluoride.

TABLE 2

Substance	Boiling point	n_D^t	d_4^{20}
3,5,5-Trimethyl-2-heptene (low boiling) [7]	160.3°	1.4367 (25°)	0.7850
3,5,5-Trimethyl-2-heptene (high boiling) [8]	162.1	1.4388 (25)	0.7756
Cis-1-phenyl-1-propene [9]	64.5 (20 mm)	1.5400 (20)	0.9107
Trans-1-phenyl-1-propene [9]	73.5 (20 mm)	1.5473 (20)	0.9019

EXPERIMENTAL

Vinylsulfonyl fluoride (I). a) To 35.8 g of β-chloroethanesulfonyl chloride [4] (b.p. 70-71° (5 mm) $n^{20}D$ 1.4910) was added 90 ml of a saturated solution of potassium fluoride, the mixture was heated in a Favorskii flask; it was gradually brought to boiling, and the distillate was collected in the range 92-99°. The organic layer of the distillate was dried over calcium chloride and gave 21.8 g of (I) (yield 45.3%).

B.p. 118-120° (747 mm), $n^{20}D$ 1.3850, d^{20}_4 1.3329, MR_D 19.37.
Found %: C 22.75, 22.76; H 3.08, 2.80; S 28.11; F 16.4, 16.6. $C_2H_3O_2SF$. Calculated %: C 22.8; H 2.73; S 29.0; F 17.2.
Literature data for (I) [3]: b.p. 44-46° (50 mm).

(I) decolorized acidified potassium permanganate solution, but did not react particularly with a solution of bromine in carbon tetrachloride.

Besides this, we isolated by distillation 3.5 g of a fraction with b.p. 170-172° (758 mm), identified as β-chloroethanesulfonyl fluoride, which was described earlier [1].

b) Under these conditions 17.2 g of vinylsulfonyl chloride (b.p. 68° (20 mm)) and 49 g of potassium fluoride gave 6 g of(I)(yield 40%).

c) 15.5 g of β-fluoroethanesulfonyl chloride (obtained according to [10])and 40 g of potassium fluoride under analogous conditions gave 4.8 g of(I)($n^{20}D$ 1.3845), and β-bromoethanesulfonyl chloride [11] gave 43% conversion to (I).

β-Chlorovinylsulfonyl chloride (II). To 50 g of β,β-dichloroethanesulfonyl chloride [6] in 100 ml of absolute ether was added over 3 hours 25 g of triethylamine in 60 ml of absolute ether, dropwise with energetic stirring and cooling to −45 to −65°. The mixture was then brought to room temperature, 50 ml of 1% sulfuric acid was added, it was cooled to 0°, the ether layer was washed once more with 1% sulfuric acid, then water and a 20% solution of sodium chloride, then dried over sodium sulfate, and distilled. We obtained(II)(12 g, that is, 30%) (in the form of a mixture of cis and trans forms) with the following constants:

B.p. 50-52° (3 mm), $n^{20}D$ 1.5043, d^{20}_4 1.5858, MR_D 30.09.
Found %: C 15.71, 15.72; H 1.43, 1.55; Cl 40.96, 40.86. $C_2H_2O_2SCl_2$. Calculated %: C 14.91; H 1.24; Cl 42.65.

β-Chlorovinylsulfonyl fluoride (III). 100 g of β,β-dichloroethanesulfonyl chloride was treated with 150 g of saturated solution of potassium fluoride as for(I); we obtained 30.7 g (40.1%) of a fraction with b.p. 34-49° (25 mm). The accumulation from several experiments of this fraction (200 g in all) was vacuum distilled in a rectifying column. The isolated fractions were: 1, b.p. 42.7-43.1° (25 mm), and 2, b.p. 45° (25 mm).

Properties of fraction 1.

M.p. −45°, $n^{20}D$ 1.4170, d^{20}_4 1.5384, MR_D 24.40.
Found %: C 16.64, 16.53; H 1.96, 1.78. $C_2H_2O_2SFCl$. Calculated %: C 16.65; H 1.38.

Properties of fraction 2.

M.p. −22.0°, $n^{20}D$ 1.4341, d^{20}_4 1.5247, MR_D 24.58.
Found %: C 16.21, 16.24; H 1.77, 1.57. $C_2H_2O_2SFCl$. Calculated %: 16.65; H 1.38.

Besides this we also isolated a substance with b.p. 69.5-70° (25 mm).

$n^{20}D$ 1.4625, d^{20}_4 1.5772, MR_D 31.74. The chlorine split by the action of an equimolecular amount of triethylamine was 19.6, 20.1%.

Found %: F 7.66, 7.87. $C_2H_3O_2SFCl_2$. Calculated %: F 10.49.

This substance was evidently β,β-dichloroethanesulfonyl fluoride [1], which contained some amount of contaminants.

SUMMARY

We have shown that the action of potassium fluoride on halogen substituted alkanesulfonyl chlorides can give sulfonyl fluorides of the unsaturated series and their halogen derivatives. By this method we have synthesized vinylsulfonyl fluoride and β-chlorovinylsulfonyl fluoride (in two stereoisomeric forms).

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THE HYDROLYSIS OF ESTERS OF AROMATIC SULFONIC ACIDS

V. THE HYDROLYSIS OF ESTERS OF BENZENESULFONIC ACID AND SUBSTITUTED PHENOLS

R. V. Vizgert

A number of factors are significant in the mechanism of hydrolysis of esters: 1) conditions of hydrolysis (nature of catalysis, solvent, etc.)[1-3]; 2) acidic properties of the constituent acid and alcohol [4]; 3) spatial distribution of branching substituents in acyl or alkyl radicals of the ester [5-7].

Increase in the acidic properties not only of the acid, but also of the alcohol increases the rate of hydrolysis [8-10], and also in a number of cases changes the mechanism of hydrolysis. In esters of carbonic acid with aliphatic and aromatic alcohols and phenols, the bond is broken at the acyl [11-13, 35]. Esters of acids of medium strength, such as phosphoric [14], nitrous [4], and aliphatic alcohols are hydrolyzed at the acyl or alkyl bond depending on the medium. Esters of strong acids like $HClO_3$ [4], benzenesulfonic [15-17] and aliphatics are hydrolyzed only on the alkyl.

The results of previous work [18-20] on the study of the effect of electrophilic and nucleophilic substituents on the rate of hydrolysis of alkyl- and arylsulfonates which contain substituents in benzenesulfonic acid show different mechanisms for their hydrolysis [21]. The behavior of alkyl- and arylsulfonates in other reactions, such as reaction with water [22], alcohols [23], phenols [24, 25], amines [26, 27], and the action of hydrogen at the moment of its evolution [28], also show differences in the lability of the bonds in alkyl- and arylsulfonates. It is interesting to see what is the effect on reaction rate and mechanism of hydrolysis of arylsulfonates depending on the introduction of different substituents in the phenol. When substituents are introduced into benzenesulfonic acid the properties of the latter are changed slightly, while electrophilic and nucleophilic substituents in the phenol should change the dissociation constant of the phenol sharply, and hence should have considerable effect on the rate of hydrolysis of the arylsulfonate. For this study we chose esters of benzenesulfonic acid and phenol with substituents in the phenol and in the sulfonic acid: o-CH_3, p-Cl, p-NO_2, 2,4-$(NO_2)_2$. The results of the experiments agreed with the data from previous work.

EXPERIMENTAL

Esters of benzenesulfonic acid with p-Cl, p-NO_2, and o-CH_3 substituted phenol were obtained by reaction of the substituted phenol with benzenesulfonic acid in an aqueous alkali medium with subsequent isolation and recrystallization [29]. The ester of 2,4-dinitrobenzenesulfonic acid and phenol was obtained from the corresponding sulfonyl chloride, which was kindly prepared for us by A. I. Tolmachev, and sodium phenolate in anhydrous alcohol [30]. The ester of 2,4-dinitrophenol and benzenesulfonic acid was obtained from the corresponding phenolate and benzenesulfonyl chloride in anhydrous alcohol. The melting points of the esters are given in Table 1.

Hydrolysis was carried out in a 70% water-dioxane medium with alkali at 50 and 70°. The initial concencentration of ester was 0.012 g mole/liter, and of KOH 0.033-0.035 g mole/liter. Hydrolysis of the ester from benzenesulfonic acid and 2,4-dinitrophenol and the ester from 2,4-dinitrobenzenesulfonic acid and phenol, because of the great rapidity, were carried out at 0 and 15°, and the initial concentration of ester was 0.0031 g mole/liter and of alkali 0.0084 g mole/liter (because of the small concentrations of ester and alkali, we used a double sample for titration).

TABLE 1

Meaning of X and Y in the formula $YC_6H_4SO_2OC_6H_4X$		Melting point
X	Y	
H	H	35—36° [27]
4-Cl	H	20—22 [29]
4-NO_2	H	84—85
2-CH_3	H	39—40
2,4-$(NO_2)_2$	H	118—119
H	2,4-$(NO_2)_2$	115—116 [34]

The rate of hydrolysis was determined by titrating the excess acid with alkali in the presence of methyl red [18-20]. For a more detailed description of the method, see [8].

The rate constants of the hydrolysis were calculated by the equation of the second order with account taken of the double cost of alkali: $dx/dt = k(a-2x)(b-x)$, where: $\underline{a}$ is concentration of alkali and $\underline{b}$ is concentration of ester. The energy of activation was calculated by the Arrhenius equation:

$$E = \frac{(\log k_2 - \log k_1) \cdot 4.575 \cdot T_1 \cdot T_2}{T_2 - T_1}$$

The pre-exponential factor was calculated by the equation $k = Pzc^{-E/RT}$.

The dimensions of the values were: $\underline{k}$ in liter/mole sec, E in cal/mole, log P_a in liter/mole sec.

TABLE 2

30°				50°			
t (min)	$a-2x$	$b-x$	k	t (min)	$a-2x$	$b-x$	k
0	0.0353	0.0125	—	0	0.0353	0.0125	—
7	0.0309	0.0102	0.0161	3	0.0275	0.0085	0.0733
10	0.0290	0.0093	0.0152	9	0.0195	0.0045	0.0727
16	0.0263	0.0079	0.0153	13	0.0167	0.0030	0.0793
24	0.0237	0.0066	0.0152	19	0.0146	0.0021	0.0753
32	0.0210	0.0053	0.0165	26	0.0134	0.0015	0.0683
45	0.0191	0.0043	0.0154	40	0.0116	0.0006	0.0885
		k_{av}	0.0156			k_{av}	0.0762

TABLE 3

50°				70°			
t (min)	$a-2x$	$b-x$	k	t (min)	$a-2x$	$b-x$	k
0	0.0353	0.0125	—	0	0.0353	0.0125	—
400	0.0328	0.0111	0.000132	60	0.0326	0.0110	0.00088
770	0.0313	0.0104	0.000116	225	0.0284	0.0089	0.00074
1355	0.0282	0.0089	0.000132	345	0.0258	0.0076	0.00089
2135	0.0256	0.0076	0.000129	444	0.0239	0.0066	0.00082
2790	0.0237	0.0066	0.000131	520	0.0223	0.0059	0.00084
		k_{av}	0.000129			k_{av}	0.00083

The results of several typical experiments on the hydrolysis of p-nitrophenyl benzenesulfonate and o-cresyl benzenesulfonate are given in Tables 2 and 3. In Table 4 we give the basic data on the hydrolysis of the arylsulfonates which we studied in this work.

For comparison of the effects of the same substituent in the benzene ring of the acid and of the alcohol on the rate of hydrolysis of the arylsulfonates, the results of the present study are compared to the kinetic data from previous work (Table 5).

TABLE 4

Value of X and Y in formula $YC_6H_4SO_2OC_6H_4X$		$k_0 \cdot 10^5$	$k_{15} \cdot 10^5$	$k_{50} \cdot 10^5$	$k_{70} \cdot 10^5$	E	$\lg Pz$
X	Y						
2-CH_3	H	—	—	0.129	0.86	20880	10.24
H	H	—	—	0.374	1.900	17860	8.66
4-Cl	H	—	—	2.47	11.23	16730	8.77
4-NO_2	H	—	—	76.65	—	15290	9.23
2,4-$(NO_2)_2$	H	339.0	830.0	—	—	9350	7.02
H	2,4-$(NO_2)_2$	38.0	183.0	—	—	16360	11.68

Discussion of Results

Electrophilic and nucleophilic substituents act in the same direction on the rate of hydrolysis, independent of their location in the benzene ring of the phenol or the benzenesulfonic acid (in Table 5 the constants for the hydrolysis of arylsulfonates are compared with the dissociation constants of the substituted phenols).

If the order of effect of the different substituents is the same, yet the relative magnitude of the effect of each of the substituents is different and depends on where the substituent is found: in the benzene ring of the acid or of the alcoholic constituent. Electrophilic substituents in the phenolic benzene ring have a greater effect on the rate of hydrolysis of arylsulfonates than when the corresponding substitution is in the benzenesulfonic acid (p-Cl, p-NO_2). The effect of electron donor substituents transmitted through the benzene ring of the phenol is weaker than the effect of these substituents in the benzene sulfonic acid. If we consider that in hydrolysis of arylsulfonates the active reaction center is the sulfur of the sulfonyl group, then the greater effect of the electrophilic substituents in the benzene ring of the phenol can be explained by the presence on the oxygen of two pairs of p-electrons which are united to the electrons of the benzene ring. Change in the energy of activation and the probability factor correspond to the change found in the rate constant. The effect of substituents in the ortho, meta, and para positions differs depending on whether the substituent is in the benzene ring of the acid or alcoholic portion.

In esters of benzenesulfonic acid and substituted phenols the nitro group follows this order in its effect on rate of hydrolysis: o-NO_2 > p-NO_2 > m-NO_2, and for esters of phenol and substituted benzenesulfonic acids, a different order: p-NO_2 > m-NO_2 > o-NO_2. Thus, the nitro group in the ortho position in benzenesulfonic acid decreases the rate of hydrolysis of arylsulfonates and aromatic sulfonyl chlorides [20], while the nitro group in the ortho position in phenols has a favorable effect, showing only its electronic action and not steric hindrance.

The methyl group in its lessening effect on the rate of hydrolysis of esters of benzenesulfonic acid and substituted phenols stands in the order o-CH_3 > p-CH_3 > m-CH_3.

The decrease in rate of hydrolysis shown by the methyl group in the ortho position can come from its electronic influence and not from a spatial effect.

The accumulation of electronegative nitro groups in benzene sulfonic acid, and especially in phenol, sharply increases the rate of alkaline hydrolysis. The ester of 2,4-dinitrophenol with benzenesulfonic acid, as distinct from the corresponding unsubstituted ester of phenol, and even from the ester of 2,4-dinitrobenzenesulfonic acid with phenol, is hydrolyzed by water, which does not occur with the latter two. When a water-dioxane solution of the ester of 2,4-dinitrophenol and benzenesulfonic acid is heated for 45 hours on the water bath at 80°, it is 45% hydrolyzed, and when heated in a sealed tube at 120° for 37 hours, 60%. Under these conditions the ester from 2,4-dinitrobenzenesulfonic acid and phenol gave only a trace (3-5%) of phenol. When phenyl benzenesulfonate was heated for 140 hours at 120° it did not even give a trace of phenol. The presence of acid as a catalyst in all cases did not affect the rate of hydrolysis. In this respect esters of 2,4-dinitrophenol and benzenesulfonic acid resemble the alkyl esters of benzenesulfonic acid (which are hydrolyzed by water and the rate of hydrolysis is considerably increased by the presence of alkali and not by the presence of acid). It is possible that further evidence of this resemblance will be found in the mechanism of hydrolysis. Comparison

TABLE 5

Value of X	$C_6H_5SO_2OC_6H_4X$			$XC_6H_4SO_2OC_6H_5$			$XC_6H_4SO_2OC_6H_4SO_2C_6H_4OH$			XC_6H_4OH
	$k_{50} \cdot 10^3$	E	lg PZ	$k_{50} \cdot 10^3$	E	lg PZ	$k_{50} \cdot 10^3$	lg PZ	E	dissociation constant
2-CH_3	0.129	20880	10.24	—	—	8.78	—	—	—	$6.3 \cdot 10^{-11}$*
4-CH_3	0.184	18500	8.78	0.145	18650	—	—	—	—	$6.7 \cdot 10^{-11}$
3-CH_3	0.263	18320	8.82	—	—	8.66	—	—	—	$9.8 \cdot 10^{-11}$
H	0.374	17860	8.66	0.374	17860	8.72	15.45	8.64	15460	$1.0 \cdot 10^{-10}$
4-Cl	2.47	16730	8.77	1.120	17190	8.92	21.70	8.81	15470	—
2-NO_2	134.9	15980	9.95	7.34	16340	7.40	—	—	—	$7.5 \cdot 10^{-8}$**
4-NO_2	76.65	15290	9.23	26.3	13160	8.35	—	—	—	$9.6 \cdot 10^{-8}$
3-NO_2	31.5	15450	8.95	11.44	15200	11.68	171.2	9.33	14890	$5.3 \cdot 10^{-9}$
2,4-$(NO_2)_2$	$k_0 = 339$	9350	7.02	$k_0 = 38.0$	16350	—	—	—	—	$1.0 \cdot 10^{-4}$
$HOC_6H_4SO_2$	15.45	15460	8.64	—	—	—	—	—	—	$2.7 \cdot 10^{-8}$***
$C_6H_5SO_2$	23.25	15110	8.60	—	—	—	—	—	—	$1.4 \cdot 10^{-8}$

*[31]. **[32]. ***[33].

of the rate constant of the hydrolysis with the dissociation constant of the corresponding phenol shows that increase in acid properties of the alcohol increases the rate of hydrolysis (Table 5). An analogous relation between rate of hydrolysis and dissociation constant occurs in the esters of benzoic acid with substituted phenols [10].

The parallel between the dissociation and hydrolysis constants confirms the assumption of Hammett [13] of the constancy of the effect of substituents transmitted through a benzene ring in different types of chemical reactions in which the substituted benzene ring takes part. However, we could not calculate the reaction constants of the hydrolysis of esters of benzenesulfonic acid with substituted phenols because of the presence of the ester oxygen which strengthened or weakened the action of the substituents.

The experimental data which we obtained (greater effect of substituents in the alcoholic portion on rate of hydrolysis of aryl sulfonates compared to the corresponding substituents in the acid portion; presence of an ortho effect when the substituent is introduced into esters of substituted benzenesulfonic acids and its absence when introduced into esters of benzenesulfonic acid with substituted phenols) confirms the mechanism of hydrolysis of aryl sulfonates with rupture of the bond sulfur-oxygen, so that the ester oxygen remains on the side of the phenolic residue, and the active center of the reaction is the sulfur of the sulfonyl group.

SUMMARY

1. We have studied the rate of alkaline hydrolysis of six esters of benzenesulfonic acid and substituted phenols.

2. Increased acidic properties of the substituted phenols increases the rate of hydrolysis of the corresponding esters of benzenesulfonic acid.

3. Electronegative substituents show a great effect on the rate of hydrolysis when in the alcoholic but not when in the acid portion of the ester.

4. Substituents in the ortho position in the benzene ring of the phenol do not show a steric effect.

5. The results confirm the mechanism of hydrolysis of aryl sulfonates in which the active center of the reaction is the sulfur of the sulfonyl group.

6. The ester of 2,4-dinitrophenol and benzenesulfonic acid as distinct from the other known esters of substituted phenols, is hydrolyzed by water.

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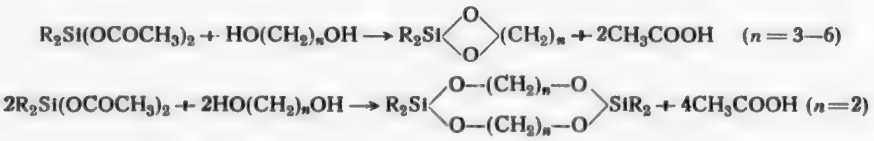
STUDIES IN THE FIELD OF ALKOXYSILANES

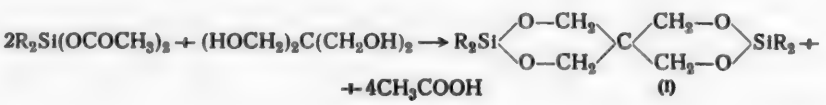
XI. REACTION OF DIALKYLDIACETOXYSILANES WITH GLYCEROL AND PENTAERYTHRITOL*

V. P. Davydova and M. G. Voronkov

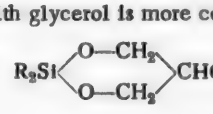
Earlier [2] we showed that dialkyldiacetoxysilanes react with glycols to form cyclic ethers of the dialkylsilanediols or their dimers.



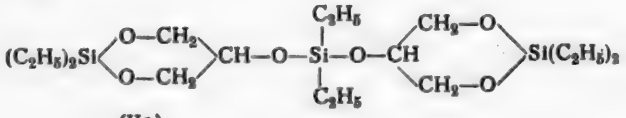
It appeared interesting to us to extend their reaction to polyatomic alcohols, especially to glycerol and pentaerythritol. We showed that dialkyldiacetoxysilanes react smoothly with pentaerythritol with the formation of the previously unknown spirocyclic ethers of dialkylsilanediol according to the scheme:



Thus, for example when pentaerythritol reacts with dimethyldiacetoxysilane, we get 88% of crystalline 3,3,9,9-tetramethyl-2,4,8,10-tetraoxa-3,9-disilaspiro(5,5)undecane (I).

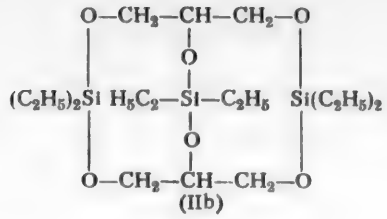
The reaction of dialkyldiacetoxysilanes with glycerol is more complex and does not lead to the formation of 2-sila-1,3-dioxolane derivatives of the type  which are described in the patent literature [3].

When diethyldiacetoxysilane reacts with glycerol we find an 80% yield of a compound which corresponds to the formula $C_{13}H_{30}O_6Si_3$ (II), for which two structures are equally possible: IIa, [diethyl-bis-(2,2-diethyl-1,3-dioxa-2-silacyclohex-5-oxy)silane] and IIb, (Si-hexaethyl-3,5,9,11,13,15-hexaoxa-4,10,14-trisilabiscyclo[5,5,3]-pentadecane). The third structure IIc is hardly possible because of the difficulty of formation of a five membered 2-sila-1,3-dioxolane ring [2].

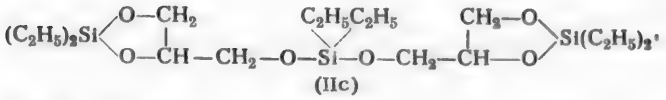


(IIa)

*Previous communication, see [1].



(IIb)



(IIc)

In contrast to this, when dimethyldiacetoxysilane reacted with glycerol, in all the experiments we obtained an easily polymerized substance of the formula $C_7H_{18}O_5Si$ which contained two hydroxyl groups and one acetoxy group united with a carbon atom.* One of the hydroxyl groups occurs on a silicon atom, as the infrared spectrum of the substance shows.** The spectrum has a very strong band at 3485 cm^{-1} which belongs to an associated OH group. In the spectrum of a 0.5% solution of the substance in CCl_4 the nature of the band is little changed (there is a slight increase in frequency) which evidently shows the presence of an intramolecular hydrogen bond. There is complex absorption in the 880-790 cm^{-1} region. However, in a 10% solution of the substance in pyridine, one of the bands (~815 cm^{-1}) is shifted because at this place passage increases. Usually the bands belonging to the oscillation of the valence group Si—OH behave thus.

All these results show that the product of the reaction of dimethyldiacetoxysilane with glycerol is dimethyl-(2-hydroxy-3-acetoxypropoxy)silanol (III). The formation of(III) can be presented in the following scheme

$$(CH_3)_2Si(OCOCH_3)_2 + HOCH_2CHOHCH_2OH \longrightarrow$$
$$\longrightarrow (CH_3)_2Si(OCOCH_3)OCH_2CHOHCH_2OH + CH_3COOH \longrightarrow$$
$$\longrightarrow (CH_3)_2Si(OCOCH_3)OCH_2CHOHCH_2OCOCH_3 + H_2O \longrightarrow$$
$$\longrightarrow (CH_3)_2Si(OH)OCH_2CHOHCH_2OCOCH_3 + CH_3COOH,$$
(III)

or as a direct intramolecular rearrangement of the primary reaction product (cf [4]).

$$(CH_3)_2Si(OCOCH_3)OCH_2CHOHCH_2OH \longrightarrow (CH_3)_2Si(OH)OCH_2CHOHCH_2OCOCH_3$$
(III)

The occurrence of an acetoxy group in compound(III) on the primary carbon atom is indicated since glycerol usually acetylates in the α-position.

EXPERIMENTAL

The starting dialkyldiacetoxysilanes were described earlier [5]. Glycerol was purified by vacuum distillation and had b.p. 155° (5 mm), $n^{20}D$ 1.4743. Pentaerythritol was recrystallized from water then dried in a vacuum oven over P_2O_5 (m.p. 260.5°).

Reaction of dimethyldiacetoxysilane with pentaerythritol. 52.9 g of dimethyldiacetoxysilane was added to 20.4 g of pentaerythritol and the mixture was stirred at 80-90° for 1 hour. The acetic acid which formed was distilled off in a vacuum and the residue was distilled at ordinary pressure. Yield of(I) with b.p. 243-245° (749 mm) was 32.8 g (88%). After two distillations in a vacuum, m.p. 136°.

*A substance which contains an acetoxy group on a silicon atom is easily hydrolyzed by water or aqueous alkali with splitting of the acetoxy group, which does not occur in this case.

**The authors are grateful to Ia. I. Ryskin for the infrared spectrum and its interpretation.

Found %: C 43.21, 43.24; H 7.97, 8.09; Si 22.21, 22.31. M 252.0, 254.2. $C_9H_{20}O_4Si_2$. Calculated %: C 43.51; H 8.11; Si 22.61. M 248.44.

Reaction of diethyldiacetoxysilane with glycerol. To a solution of 39.8 g of diethyldiacetoxysilane in 100 ml of absolute ether was added 12.0 g of glycerol and the reaction mixture was stirred for 3 hours. After distillation of the ether, the residue was vacuum distilled. Besides acetic acid we obtained 22.8 g of(II)with b.p. 230-245° (14 mm). Yield 80%. A colorless, viscous liquid with a boiling point after repeated distillation of 230-233° (14 mm).

d^{20}_4 1.0521, $n^{20}D$ 1.4605.

Found %: C 49.86, 49.99; H 9.50, 9.69; Si 19.27, 19.19. M 439.9, 433.1. $C_{18}H_{40}O_6Si_3$. Calculated %: C 49.50; H 9.23; Si 19.29. M 436.78.

Reaction of glycerol with dimethyldiacetoxysilane. To 67 g of dimethyldiacetoxysilane was added with stirring 23 g of glycerol. After stirring 10 minutes at room temperature, the reaction mixture warmed spontaneously to 50°. With further stirring it set to a clear, viscous mass which was dissolved by adding 70 ml of absolute ether. After distillation of the ether the reaction mass was distilled in a vacuum. We thus obtained 41 g of(III)(yield 79% calculated on the starting glycerol). B.p. 102-133° (10 mm); after a second distillation, b.p. 125-130° (10 mm).

d^{20}_4 1.1432, $n^{20}D$ 1.4450.

Found %: C 41.30, 41.60; H 7.87, 8.03; Si 13.48, 13.29; $OCOCH_3$ 27.95, 28.07; H(O) 0.74. M 313.2, 325.2. $C_7H_{16}O_5Si$. Calculated %: C 40.36; H 7.74; Si 13.48; $OCOCH_3$ 28.36; H(O) 0.97. $(C_7H_{16}O_5Si)_{1.5}$. Calculated: M 312.44.

The substance was a colorless, viscous liquid, especially unstable when kept and easily polymerized, which makes its analysis difficult. The substance was dissolved in water; the water solution had a neutral reaction. After 12 hours in a sealed ampoule, the substance was converted into a clear, glassy resin. This resin distilled without decomposition at 162-184° (4 mm), passing over as a viscous liquid which quickly set again to the resin with the same properties. The results of a molecular weight determination in dioxane showed that the substance was associated (degree of association 1.5).

In another experiment, in which the molar ratio of the starting substances was 1 : 1, we also obtained substance(III)with a yield of 72%. B.p. 155-160° (15 mm), $n^{20}D$ 1.4460.

SUMMARY

The reaction of dialkyldiacetoxysilanes with pentaerythritol leads to formation of a spirocyclic ether of dialkylsilanediol. Diethyldiacetoxysilane and dimethyldiacetoxysilane react differently with glycerol, forming in the first case a bicyclic ether of diethylsilanediol, and in the second, an acyclic monoether of dimethylsilanediol with α-acetyl.

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THE SPLITTING OF MACROTOMINIC ACID AND ACIDS FROM HELIOSUPINE IN CAUSTIC ALKALI SOLUTIONS

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Macrotominic acid was first observed in a study of the alkaloid macrotomine as an ester of this acid and the aminoalcohol trachelanthamidine. However, the acid was so strongly decomposed when the alkaloid was saponified by caustic alkalis that it could not be obtained in pure form. Therefore, for a study of its structure the free acid was not used, but macrotomine itself; and on the basis of a study of the products of its oxidative decomposition by its reaction with iodic acid, it was shown with great probability that macrotominic acid has the structure 2-methyl-2,3,4-trihydroxypentane-3-carboxylic acid (I) [1]. Thus, the structure of macrotominic acid differs from lasiocarpic and only in that it has a hydroxyl group in position 4 instead of a methoxyl [2].

Lasiocarpic acid also is not obtained by saponifying the alkaloid, but it can easily be obtained in pure form by reducing lasiocarpine with a platinum catalyst. This reduces the allyl hydroxyl group which is esterified with lasiocarpic acid.

Macrotomine, an ester of the saturated amino alcohol trachelanthamidine, cannot be catalytically reduced to give a free acid of the structure 2-methyl-2,3,4-trihydroxypentane-3-carboxylic acid. However, such a possibility exists, due to the discovery of the new alkaloid, heliosupine. This alkaloid is very close in structure to lasiocarpine and differs from it only in that the primary hydroxyl group of heliotridine (allyl) is esterified not with lasiocarpic acid, but with an acid which has the same structure as macrotominic acid [3]. Naturally, we can expect to obtain from this alkaloid the free acid under conditions for obtaining lasiocarpic acid from lasiocarpine.

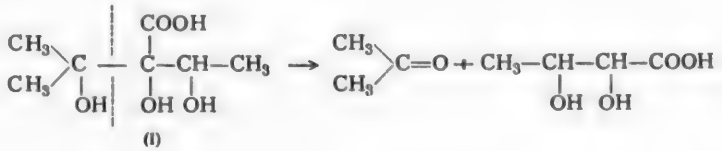
Actually, when heliosupine is reduced with a platinum catalyst it gives a free acid which is characterized as the quinine salt, m.p. 186° (the free acid does not crystallize).

From the products of splitting macrotominic acid obtained by alkaline hydrolysis of the alkaloid macrotomine was isolated acetone and an optically inactive acid with the composition $C_4H_8O_4$. This was isolated as its quinine salt with m.p. 173-174° and with $[\alpha]_D$ −104° (water).

These constants are very close to those for the quinine salt of the high melting inactive form of α,β-dihydroxybutyric acid (m.p. 174°, $[\alpha]_D$ −108° [4]). However, the latter in the free form is described as a well crystallized substance with a melting point about 80°, while our acid does not crystallize.

To confirm the composition of our acid we must find a simpler salt with a lower molecular weight than the quinine salt. The well crystallized sodium salt was such a one; analysis of this salt confirms the composition $C_4H_8O_4$ for the acid, that is, the composition of dihydroxybutyric acid.

A comparison of these results with the structural formula for macrotominic acid gives the important conclusion that splitting of the latter takes place by rupture of the C−C bond between the 2nd and 3rd carbon atoms, occurring because of transfer of a hydrogen atom from the hydroxyl group in position 2 to the carbon atom in position 3.



(I)

As our investigation showed, lasiocarpic acid undergoes an analogous split. Also we found for lasiocarpic acid that the rate of its splitting depends to a considerable extent on whether the free acid (more exactly, its salt) or its ester is submitted to the action of an alkaline solution. In the case of the ester splitting goes about 200 times faster than in the case of the salt [5].

Obtaining a free acid with the structure of 2-methyl-2,3,4-trihydroxypentane-3-carboxylic acid from heliosupine made it possible to confirm this finding and to judge the degree of its splitting by the amount of acetone evolved. It was shown that this acid is also split very slowly when it is heated in an alkaline solution, while the analogous action of alkali on macrotomine and heliosupine gives a much faster splitting.

The very small amount of heliosupine which we had at our disposal did not permit us to obtain sufficient free acid to synthesize its pure methyl ester. The inability to crystallize it also made its purification difficult. Yet even the work with the impure ester obtained by the action of diazomethane on the acid showed that the rate of its splitting was increased compared to that of the free acid and was very close to the rate of splitting of the methyl ester of lasiocarpic acid.

EXPERIMENTAL

Splitting of macrotominic acid in the saponification of macrotomine. 5 g of the alkaloid was dissolved in 40 ml of 1 N sodium hydroxide solution and the solution was heated for 1 hour in a sealed ampoule on a boiling water bath. Then the ampoule was carefully cooled and its contents transferred to a Wurtz flask. The ampoule was washed with 20 ml of water, the wash water was combined with the alkaline solution, and 25 ml of water was distilled from the combined solutions in order to estimate the acetone which was formed. Concentrated hydrochloric acid was added to the distillate in such amount that the acid concentration was about that of a 2N solution. Then a solution saturated at 20° with 2,4-dinitrophenylhydrazine was added to the 2 N hydrochloric acid solution to complete precipitation of the acetone. We obtained 3.55 g (89.9%) of acetone dinitrophenylhydrazone. The residual alkaline mother liquors after the acetone had been distilled off were extracted with chloroform to complete removal of the amino alcohol (trachelanthamidine), and after carbon dioxide gas has been passed in, the water was completely distilled off in a vacuum. The dry residue was extracted with boiling anhydrous alcohol. The inorganic salts were filtered from the alcohol solution, and the solvent was distilled from it. The residue was dissolved in 50 ml of water and the solution was passed through a column of ion exchange resin (cationite p, phenolic). After the solution was dried in a vacuum, the quinine salt was obtained from the noncrystallizing acid. For this the acid was dissolved in a small amount of alcohol and to the solution dry quinine was added until the acid reaction disappeared. The salt was separated from the solution by adding a large amount of dry ether. The precipitate was washed with ether and recrystallized from dry acetone. After two recrystallizations the salt melted at 173-174°, $[\alpha]_D^{16}$ −104° (c 5.00, water).

Found %: C 64.74, 64.76; H 7.48, 7.52; N 6.28. $C_{24}H_{32}O_6N_2$. Calculated %: C 64.82; H 7.27; N 6.30.

Sodium salt. 1.2 g of the quinine salt was dissolved in 30 ml of water and the solution was passed through a column filled with ion exchange resin (cationite p,phenolic). The resulting acid solution was treated with an excess of sodium bicarbonate and evaporated to dryness in a vacuum. The dry residue was extracted with boiling anhydrous alcohol. The alcohol solution was filtered and concentrated to small volume. Addition of ether to the concentrated alcohol solution gave a crystalline precipitate (after recrystallization from alcohol, white, glittering plates).

Found %: C 33.35, 33.63; H 4.85, 4.73. $C_4H_7O_4Na$. Calculated %: C 33.80; H 4.92.

The salt was optically inactive.

Judging by the amount of acetone formed in the saponification of heliosupine we concluded that in this case the acid underwent an analogous splitting.

Obtaining a free acid from heliosupine. Heliosupine, obtained from 10 g of the crystalline picrate, was dissolved in 40 ml of 0.5 N hydrochloric acid solution and to the solution was added the catalyst (from 1 g of H_2PtCl_6) and the mixture was shaken at a small excess pressure in an atmosphere of hydrogen. About 3 g moles of hydrogen were rapidly absorbed. The acid solution was filtered from the catalyst, neutralized with soda, and evaporated dry. The residue was extracted with boiling anhydrous alcohol. The alcohol was completely distilled from the solution and the residue was dissolved in 150 ml of water. The water solution was passed through a column with a cationite

resin (espatite). After the passage of all the solution, the column was washed with water. The solution and the wash water were combined and evaporated dry in a vacuum. There remained a colorless, noncrystalline mass whose water solution rotated a plane of polarized light to the right.

To characterize the noncrystalline free acid we prepared its quinine salt. To an alcohol solution of the acid we gradually added dry quinine to a full alkaline reaction and precipitated the quinine salt with absolute ether. After reprecipitation from alcohol solution by ether the salt appeared as snow white, silky needles with m.p. 186°, $[\alpha]_D^{20}$ −105° (c 6.46, alcohol).

Found %: C 64.34, 64.48; H 7.61, 7.66; N 5.74, 5.89; OH 17.23, 16.70. $C_{27}H_{33}O_7N_3$. Calculated %: C 64.47; H 7.62; N 5.57; OH 16.92.

Splitting of the acid from heliosupine by alkaline solution. 1 g of the acid obtained from the quinine salt by passing its water solution through a cationite resin (espatite) was heated in a sealed ampoule at 100° in 20 ml of 1 N sodium hydroxide for 4 hours. All further operations in the determination of the amount of acetone formed were carried out in the same way as in the case of splitting of macrotomine. We obtained 0.028 g (2.09%) of acetone 2,4-dinitrophenylhydrazone.

SUMMARY

In the alkaline splitting of macrotomine and heliosupine which are esters of an acid with the structure 2-methyl-2,3,4-trihydroxypentane-3-carboxylic acid [1], the latter was quickly split into acetone and dihydroxybutyric acid. This splitting also occurs in the heating in alkaline solution of the free acid from heliosupine (more correctly, its salt) but it goes much more slowly (about 200 times less).

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**In Russian.

INTERMEDIATE PRODUCTS IN THE CONDENSATION REACTION OF ISOAMYL ALCOHOL

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In the reaction of isovaleric aldehyde with solutions of sodium isoamylate in isoamyl alcohol [1] two unsaturated alcohols are formed: 2,6-dimethyl-3-methylol-4-heptene and 2,6-dimethyl-3-methylol-3-heptene. From these alcohols there is gradually formed 2,6-dimethyl-3-methylolheptane, which is the condensation product of isoamyl alcohol in the presence of its alcoholate [2]. It is natural to expect that when the latter reaction proceeds, the intermediate products will be the same two unsaturated alcohols and not one, as had been assumed, for example, in the scheme suggested by one of us [3], and also in a very similar later scheme [4].

In the present work we carry out the condensation of isoamyl alcohol in the presence of its alcoholate and a dehydrogenation catalyst. Investigation of the reaction products showed that in them, besides the basic reaction product, 2,6-dimethyl-3-methylolheptane, there were present in about equal amounts both of the above mentioned unsaturated alcohols.

EXPERIMENTAL

The condensation of isoamyl alcohol was carried out in the apparatus used by us for the condensation of n-butanol. It was filled with 2500 g of isoamyl alcohol, 90 g of sodium hydroxide, and 170 g of catalyst (nickel on aluminum oxide). The length of the condensation was 40 hours; the temperature of the reaction mass at the beginning of the process was 120°, and at the end, 137°. As a result of formation of the alcoholate and condensation of the alcohol, 168 g of water was formed; 93 liters of hydrogen were obtained. The reaction product was steam distilled and the distilled alcohols were separated from the water and from unreacted isoamyl alcohol (1359 g). Besides this, 24 g of isoamyl alcohol with a content of 44% isovaleric aldehyde was separated from the water layer after running the condensation.

Rectification of the condensation product. The alcohols obtained after distilling off the isoamyl alcohol, in the amount of 674 g, were carefully fractionated in a vacuum in a column filled with Raschig glass rings. The effectiveness of the column was about 20 theoretical plates. The resulting fractions were then rectified in a vacuum on a column with the effectiveness of 11 theoretical plates. In the fractions obtained by the second fractionation we determined the specific gravity, refractive index, and bromine and hydroxyl numbers, and from these data constructed a curve of distillation. On the basis of this curve we could determine the amounts of each of the alcohols which were formed. The yields of alcohols are given in the Table. The groups of fractions with

Alcohols Obtained by the Condensation of Isoamyl Alcohol

Name of alcohol	Yield (in %)	Boiling point (pressure in mm)	d_4^{20}	n_D^{20}
2,6-Dimethyl-3-methylol-4-heptene	105	201—202° (762)	0.8348	1.4443
2,6-Dimethyl-3-methylol-3-heptene	100	203.5—205 (748)	0.8485	1.4520
2,6-Dimethyl-3-methylolheptane	360	207.5—208 (729)	0.8345	1.4369

similar properties were submitted to a supplementary vacuum rectification on a column in order to separate pure components. The properties of the resulting substances are given in the same table. The boiling points at atmospheric pressure were determined by distillation of the substances in a Wurtz flask.

2,6-Dimethyl-3-methylol-4-heptene. We obtained 35 g in pure form.

Found %: C 76.89; H 13.04; OH 10.51. Bromine No. 1032. $C_{10}H_{19}OH$. Calculated %: C 76.86; H 12.91; OH 10.89. Bromine No. 1024.

α-Naphthylurethane, m.p. 64.5-65°. Mixed m.p. with the form obtained earlier [1] gave no depression.

2,6-Dimethyl-3-methylol-3-heptene. We obtained 20 g in pure form.

Found%: C 76.64; H 12.83; OH 10.67. Bromine No. 1033. $C_{10}H_{19}OH$. Calculated %: C 76.86; H 12.91; OH 10.89. Bromine No. 1024.

2,6-Dimethyl-3-methylolheptane. We obtained it in small amount in comparatively pure form.

Found %: C 75.94; H 14.03; OH 10.51. Bromine No. 12. $C_{10}H_{21}OH$. Calculated %: C 75.88; H 14.01; OH 10.74. Bromine No. 0.

The major portion of the 2,6-dimethyl-3-methylolheptane, which contained small amounts of the unsaturated alcohols and higher boiling alcohols, was submitted to catalytic hydrogenation and subsequent rectification. We then obtained 2,6-dimethyl-3-methylolheptane with the following constants: d^{20}_4 0.8345, $n^{20}D$ 1.4370.

The constants of all three alcohols were close to those found earlier [1].

SUMMARY

We have studied the condensation of isoamyl alcohol in the presence of its alcoholate and a dehydrogenation catalyst. In the reaction product we find 2,6-dimethyl-3-methylolheptane and two isomeric unsaturated alcohols: 2,6-dimethyl-3-methylol-4-heptene and 2,6-dimethyl-3-methylol-3-heptene.

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TRICHLOROISOPHOSPHAZOACYLS OF THE AROMATIC SERIES

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There were prepared recently some trichloroisophosphazoacyls by the following reaction scheme:

$$RCONH_2 + PCl_5 \rightarrow 2HCl + RCON{=}PCl_3 \quad (1)$$

$$RCON{=}PCl_3 + HCOOH \rightarrow HCl + CO + RCONHPOCl_2 \quad (2)$$

$$RCONHPOCl_2 + PCl_5 \rightarrow POCl_3 + RCCl{=}NPOCl_2, \quad (3)$$

where: R = CCl_3 [1], $(C_6H_5)_2ClC$ & p-$NO_2C_6H_4$ [2].

It was interesting to determine whether or not reaction (3) is general or whether it is applicable only to carboxylic acids with a radical having clearly expressed electronegative character. It turned out that reaction (3) does have a general character for acids of the aromatic series. There was prepared with almost quantitative yields a number of trichlorophosphazoacyls of the type $RCCl{=}NPOCl_2$, where R = C_6H_5, p-$CH_3C_6H_4$, α- and β-$C_{10}H_7$, o- and p-ClC_6H_4, 2,4-$Cl_2C_6H_3$, o-, m- and p-$O_2NC_6H_4$, 3,5-$(O_2N)_2C_6H_3$ and m-$C_6H_4(CCl{=}NPOCl_2)_2$ (Table 1).

Reaction (3) proceeds considerably less rapidly and at a higher temperature than does reaction (1) [3]. The absorption of heat [4] which is characteristic of reaction (1) is not observed in reaction (3). The reaction (3) resembles in its character the reaction of phosphorus pentachloride with N,N-dialkylamides of carboxylic acids [5].

Trichloroisophosphazoacyls of the aromatic series are liquid or low melting crystalline substances. They lose phosphorus oxychloride on being heated and yield nitriles according to the scheme:

$$RCCl{=}NPOCl_2 \rightarrow POCl_3 + RCN \quad (4)$$

However, reaction (4) proceeds considerably slower and at much higher temperatures than the thermal decomposition of trichlorophosphazoacyls [3] according to scheme (5) (Table 1 and Table 2).

$$RCON{=}PCl_3 \rightarrow POCl_3 + RCN \quad (5)$$

Thus the jump of chlorine proceeds noticeably more difficultly than the jump of oxygen. This is evidently explained by the fact that in the reaction (5) there occurs a replacement of N=P bond by a thermodynamically much more advantageous O=P bond, while in reaction (4) there occurs the replacement of N=P bond by Cl−P bond, the energy difference of which is considerable smaller.

Trichloroisophosphazoacyls are quite stable in the absence of moisture and may be stored in tightly closed vessels at room temperature for many months without change. They are rapidly hydrolyzed by the action of atmospheric moisture. Hydrolysis of trichloroisophosphazoacyls by means of formic acid proceeds in a more complex manner, in contrast to the analogous reaction of trichlorophosphazoacyls [6], and yields waxy substances the nature of which has not been studied so far. Trichloroisophosphazoacyls react just as energetically with alcohols, water, ammonia, amines, phenols and other substances containing active hydrogen atoms, as do trichlorophosphazoacyls. Therefore, trichloroisophosphazoacyls may serve as the starting materials for the preparation of varied derivatives of phosphoric acid of new types, these being the corresponding derivatives of the reactants listed above.

Several previously undescribed trichlorophosphazoacyls and dichlorides of acylamidophosphoric acids were synthesized for use as starting materials, as were the corresponding acylamidophosphoric acids.

EXPERIMENTAL

General method of preparation of trichloroisophosphazoacyls [by scheme (3)]. A mixture of 0.05 mole of the dichloride of the appropriate acylamidophosphoric acid and 0.051 mole of powdered phosphorus pentachloride (in case of the tetrachloride of isophthaloylbisamidophosphoric acid there was used 0.102 mole) was heated on an oil bath at 125-135° until hydrogen chloride evolution stopped completely, which required 20-25 minutes. During this time some 85-95% of the theoretical amount of hydrogen chloride was formed. Phosphorus oxychloride was distilled in vacuum. The residue contained trichloroisophosphazoacyls in the form of colorless transparent viscous liquids which on being cooled to −70° were transformed into glassy transparent fragile masses. The yields were almost quantitative. Trichloroisophosphazo-p-nitrobenzoyl [2] and trichloroisophosphazo-3,5-dinitrobenzoyl are crystalline substances.

All the trichloroisophosphazoacyls are rather readily soluble in benzene, more difficultly in carbon tetrachloride and petroleum ether. For analytical data see Table 1.

Thermal decomposition of trichloroisophosphazoacyls [by scheme (4)]. Into a Claisen flask with two thermometers there was charged 0.02 mole of trichloroisophosphazoacyl. The bulb of one thermometer was immersed into the substance while the bulb of the other was in the vapor space. The flask contents were gradually heated on an oil bath. The decomposition proceeds in the interval of 130-200° depending on the nature of the trichloroisophosphazoacyl compound and is terminated in 30-40 minutes. During this interval from 65 to 95% of phosphorus oxychloride distills. In some cases the mixture of the products of decomposition was distilled in vacuum for the complete removal of phosphorus oxychloride.

The yields of the nitriles, after water washing, were almost quantitative. The identification of the nitriles and $POCl_3$ were done by the usual methods.

Preparation of trichlorophosphazoacyls [by scheme (1)]. A mixture of 0.03 mole of an amide of carboxylic acid, 0.031 mole of phosphorus pentachloride and 100 ml of carbon tetrachloride were refluxed until the evolution of hydrogen chloride was complete, which requires 20-25 minutes. Carbon tetrachloride was distilled in vacuum. Trichlorophosphazoacyls remain in the residue; yields – about 100%. The following compounds were obtained in this fashion.

Trichlorophosphazo-p-toluyl, a viscous liquid, which changed to a fragile glassy mass on being chilled to −70°; it is readily soluble in benzene and carbon tetrachloride; difficultly soluble in ether and petroleum ether.

Found %: Cl 38.91; P 11.56. Equivalent after hydrolysis 4.91. $C_8H_7ONPCl_3$. Calculated %: Cl 39.44; P 11.47. Equivalent after hydrolysis 5.00.

Trichlorophosphazo-α-naphthoyl crystallizes from petroleum ether in fused needles, m.p. 66-68°; it is readily soluble in benzene, less readily in carbon tetrachloride, ether, dioxane, and petroleum ether.

Found %: Cl 34.81; P 10.62. Equivalent after hydrolysis 4.98. $C_{11}H_7ONPCl_3$. Calculated %: Cl 34.70; P 10.10. Equivalent after hydrolysis 5.00.

Trichlorophosphazo-β-naphthoyl, a viscous liquid which crystallizes to fused needles on being chilled to −35° to −40°; readily soluble in benzene and carbon tetrachloride, and difficultly soluble in ether and petroleum ether.

Found %: Cl 34.61; P 10.00. Equivalent after hydrolysis 4.93. $C_{11}H_7ONPCl_3$. Calculated %: Cl 34.70; P 10.10. Equivalent after hydrolysis 5.00.

Trichlorophosphazo-2,4-chloronitrobenzoyl, described previously as a light yellow liquid [3], crystallized after shaking with petroleum ether and chilling; m.p. 62-64°; large, almost colorless prisms (from petroleum ether). Readily soluble in benzene and carbon tetrachloride; less readily soluble in ether and petroleum ether.

Found %: hydrolyzable Cl 31.58; P 9.31. Equivalent after hydrolysis 5.02. $C_7H_3O_3N_2PCl_4$. Calculated %: hydrolyzable Cl 31.68; P 9.22. Equivalent after hydrolysis 5.00.

TABLE 1

Trichloroisophosphazoacyls of Type $RCCl{=}NPOCl_2$

R	Appearance	Found			Empirical formula	Calculated* (in %)		Thermal decomposition by scheme (4)			
		Cl (%)	P (%)	acid equiv. after hydrol.		Cl	P	temp.	time of cleavage (in minutes)	yield of $POCl_3$ (in %)	yield of RNC (in %)
C_6H_5	Viscous liquid	41.00	12.11	4.97	$C_7H_5ONPCl_3$	41.49	12.10	210—215°	30	91.4	82.4
p-$CH_3C_6H_4$	„ „	39.75	11.45	4.87	$C_8H_7ONPCl_3$	39.32	11.45	200—205	25	78.4	96.4
α-$C_{10}H_7$	„ „	34.52	10.12	5.01	$C_{11}H_7ONPCl_3$	34.70	10.10	135—140	10	88.6	86.4
β-$C_{10}H_7$	„ „	34.31	10.26	4.91	$C_{11}H_7ONPCl_3$	34.70	10.10	140—150	10	65.5	91.9
o-ClC_6H_4	„ „	36.76 **	10.65	4.91	$C_7H_4ONPCl_4$	36.59 **	10.65	175—185	40	95.0	98.3
p-ClC_6H_4	„ „	36.41 **	10.60	5.01	$C_7H_4ONPCl_4$	36.59 **	10.65	210—215	35	91.5	100.0
2,4-$Cl_2C_6H_3$	„ „	32.61 **	9.50	4.98	$C_7H_3ONPCl_5$	32.71 **	9.52	175—180	40	75.6	99.0
o-$NO_2C_6H_4$	„ „	35.32	10.11	4.89	$C_7H_4O_3N_2PCl_3$	35.30	10.28	130—135	40	86.7	100.0
m-$NO_2C_6H_4$	„ „	35.43	10.38	5.01	$C_7H_4O_3N_2PCl_3$	35.30	10.28	180—190	80	82.6	100.0
p-$NO_2C_6H_4$	Prisms *** m. p. 121—124°	35.52	10.25	4.93	$C_7H_4O_3N_2PCl_3$	35.30	10.28	215—220	40	88.4	94.5
3,5-$(NO_2)_2C_6H_3$	Prisms **** m. p. 82—84°	30.21	8.88	4.86	$C_7H_3O_5N_3PCl_3$	30.72	8.94	180—190	20	91.6	95.8
2,4-$ClNO_2C_6H_3$	Viscous liquid	31.20 **	9.25	4.91	$C_7H_3O_3N_2PCl_4$	31.68 **	9.22	170—180	15	86.7	90.1
m-$C_6H_4(CCl{=}NPOCl_2)_2$	„ „	49.10	14.61	10.00	$C_8H_4O_2N_2P_2Cl_6$	48.90	14.26	135—140	10	91.6	93.9

*For all (except the last compound) the calculated equivalent is 5.00 after hydrolysis, for the last compound it is 10.00.

**Hydrolyzable chlorine;

***Recrystallized from mixture of benzene and petroleum ether.

****Recrystallized from petroleum ether.

Bis-trichlorophosphazoisophthaloyl. A mixture of 0.03 mole of isothalic diamide, 0.062 mole of phosphorus pentachloride and 80 ml of carbon tetrachloride refluxed until the evolution of hydrogen chloride was complete, required 2-2.5 hours for this reaction. Carbon tetrachloride was distilled in vacuum and the solid residue (yield 100%) was recrystallized from petroleum ether. Large colorless prisms, m.p. 96-99°; readily soluble in benzene, somewhat less readily in carbon tetrachloride, difficultly soluble in ether and petroleum ether.

Found %: Cl 48.72; P 14.32. Equivalent after hydrolysis 9.99. $C_8H_4O_2N_2P_2Cl_6$. Calculated %: Cl 48.90; P 14.26. Equivalent after hydrolysis 10.00.

Thermal cleavage of trichlorophosphazoacyls [by scheme (5)] in contrast to the thermal cleavage of trichloroisophosphazoacyls [by scheme (4)] is an exothermic reaction. The substance is placed into a small Claisen flask and is slowly heated on an oil bath. As soon as the decomposition starts, the flask is removed from the oil bath. Even then the temperature of the reaction mixture rises by 10-30° from the heat of reaction. After the temperature ceases to rise, the flask is again immersed in the oil bath and after several minutes the reaction mixture is distilled in vacuum through a small column. The nitriles and phosphorus oxychloride were identified by the usual methods. The yields were almost quantitative. The temperatures of initiation of decomposition are given in Table 2.

TABLE 2

Thermal Decomposition of Trichlorophosphazoacyls of Type RCON : PCl_5 According to Scheme (5)

R	M. p.	Temp. of start of decomp.	R	M. p.	Temp. of start of decomp.
C_6H_5	60—61° [3]	135—136°	o-$NO_2C_6H_4$	Liquid	115—120°
p-$CH_3C_6H_4$	Liquid	120—130	m-$NO_2C_6H_4$	103—105°	125—130
α-$C_{10}H_7$	66—68	125—130	p-$NO_2C_6H_4$	121—123	125—130
β-$C_{10}H_7$	—40—35	90—100	3,5-$(NO_2)_2C_6H_3$	125—126	135—140
o-ClC_6H_4	Liquid	100—105	2,4-$ClNO_2C_6H_3$	62—64	100—105
p-ClC_6H_4	62—63	105—110	$C_6H_4(CON{=}PCl_3)_2$	96—99	125—130
2,4-$Cl_2C_6H_3$	Liquid	120—125			

Preparation of dichlorides of acylamidophosphoric acids [by scheme (2)] was run by the previously described general method [6]. All these products were difficultly soluble in benzene and carbon tetrachloride and insoluble in petroleum ether.

Dichloride of p-toluylamidophosphoric acid, yield 93.4%, prisms, m.p. 99-101°.

Found %: Cl 28.00; P 12.23. Equivalent after hydrolysis 3.98. $C_8H_8O_2NPCl_2$. Calculated %: Cl 28.13; P 12.29. Equivalent after hydrolysis 4.00.

Dichloride of α-naphthoylamidophosphoric acid, yield 84.2%; colorless large prisms; m.p. 99-101° (the melt has bright raspberry color).

Found %: Cl 24.70; P 10.81. Equivalent after hydrolysis 4.00. $C_{11}H_8O_2NPCl_2$. Calculated %: Cl 24.61; P 10.75. Equivalent after hydrolysis 4.00.

Dichloride of β-naphthoylamidophosphoric acid, yield 90.7%; prisms; m.p. 111-113°.

Found %: Cl 24.52; P 10.80. Equivalent after hydrolysis 3.96. $C_{11}H_8O_2NPCl_2$. Calculated %: Cl 24.61; P 10.75. Equivalent after hydrolysis 4.00.

Tetrachloride of isophthaloylbis-amidophosphoric acid, yield 95.6%; prisms, m.p. 130-131°.

Found %: Cl 35.41. Equivalent after hydrolysis 8.10. $C_8H_6O_4N_2P_2Cl_4$. Calculated %: Cl 35.62. Equivalent after hydrolysis 8.00.

Acylamidophosphoric acids of type $RCONHPO(OH)_2$ were prepared from the dichlorides of acylamidophosphoric acids by the previously described method [7].

p-Toluylamidophosphoric acid, yield quantitative, crystallizes in plates; m.p. 158-159°; readily soluble in water, acetone and alcohol; difficultly soluble in benzene and carbon tetrachloride.

Found %: P 14.49. Equivalent 1.98. $C_8H_{10}O_4NP$. Calculated %: P 14.40. Equivalent 2.00.

α-Naphthoylamidophosphoric acid, yield almost quantitative; crystallized in prisms; m.p. 139-141°.

Found %: P 12.21. Equivalents 1.98. $C_{11}H_{10}O_4NP$. Calculated %: P 12.33. Equivalents 2.00.

β-Naphthoylamidophosphoric acid, yield quantitative; microcrystalline powder; m.p. 155-157°.

Found %: P 12.30. Equivalents 1.98. $C_{11}H_{10}O_4NP$. Calculated %: P 12.33. Equivalents 2.00.

α- and β-Naphthoylamidophosphoric acids are readily soluble in alcohol, dioxane, acetone; less readily soluble in water; sparingly soluble in benzene and carbon tetrachloride; insoluble in ether and petroleum ether.

We failed to prepare the free isophthaloylbisamidophosphoric acid since in the hydrolysis of its tetrachloride there occurred the cleavage of phosphoric acid and there formed only the diamide of isophthalic acid.

SUMMARY

The reaction of preparation of trichloroisophosphazoacyls from the dichlorides of acylamidophosphoric acids and phosphorus pentachloride is a general reaction for the aromatic series. Several trichloroisophosphazoacyls of the aromatic series were prepared and their properties were described.

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BIS-TRIARYLOXYPHOSPHAZO-SULFONES AND TETRAARYL ESTERS OF SULFAMIDOBISPHOSPHORIC ACID

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Only bis-trichlorophosphazo-sulfone [1] has been described thus far among the possible derivatives of sulfamidobisphosphoric acid. Neither bis-triaryloxyphosphazo-sulfones nor esters of sulfamidobisphosphoric acids have been known up to the present time.

Bis-trichlorophosphazo-sulfone reacts energetically with phenolates. On mixing dry phenolates with bis-trichlorophosphazo-sulfone the reaction mixture heats up so much that smoke forms and the reaction mixture chars. In the presence of solvents, such as benzene or ether, the reaction proceeds more peacefully with formation of the corresponding bis-triaryloxyphosphazo-sulfones (I) (hexaesters of bis-trihydroxyphosphazosulfone) according to the following scheme:

$$SO_2(N{=}PCl_3)_2 + 6NaOAr \longrightarrow SO_2[N{=}P(OAr)_3]_2 + 6NaCl \qquad (II)$$

The reaction of formation of substances (I) is formally quite analogous to the reaction of formation of triaryloxy- or trialkoxyphosphazosulfonalkyls [2] or -aryls [3] (triesters of trihydroxyphosphazosulfonalkyls and aryls) (III) according to the following scheme:

$$RSO_2N{=}PCl_3 + 3NaOAr \longrightarrow RSO_2N{=}P(OAr)_3 + 3NaCl \qquad (IV)$$

However the realization of reaction (II) turned out to be incomparably more complex and difficult than was the realization of reaction (IV). Single-type substances (III), as a rule, were prepared by the same technique with closely similar yields [2, 3]. It was practically impossible to obtain the single-typed substances (I) by the same technique. In the preparation of substances (III) the purity of the starting materials and the details of the reaction conditions do not have a great significance; however, in the preparation of substances (I) the most insignificant contamination of the initial arylates and the most insignificant changes in the conditions of the reaction lead to a severe decline of the quality of the resulting reaction products, especially true for hexanaphthyl and hexatolyl derivatives. This is mainly explained by the considerably greater reactivity of substances (I) in comparison with substances (III), by the high adsorptional ability of solid substances (I) and, most importantly, by the deep-seated principal difference in the nature of these substances despite their formal resemblance, since (I) are derivatives of sulfamide while (III) are derivatives of amides of aryl- or alkylsulfonic acids (see below). Therefore for each specimen of (I) it was necessary to find special conditions of synthesis and purification and, in some cases, it was necessary to use special methods of preparation and purification of the starting arylates. Compounds (I) of type $SO_2[N{=}P(OAr)_3]_2$, with Ar: C_6H_5 (V), o-, m- and p-$CH_3C_6H_4$ (VI, VII, VIII), α- and β-$C_{10}H_7$ (IX) and (X), p-ClC_6H_4 (XI) and p-$O_2NC_6H_4$ (XII), were prepared by scheme (II).

All the (I) thus prepared were colorless substances of neutral character. Their structure is proved sufficiently regidly by the almost quantitative yield (with example of V), by the analytical data and by the transformation into tetraesters of N,N'-sulfamidobisphosphoric acid (XIV, see below). Despite the large molecular weight (from 712 to 1012) all (I) crystallize well although some of them do so very slowly. Solubility, melting point and other physical and chemical properties are determined largely by the type of the aryl group which is present in the molecule and these vary from compound to compound within rather wide limits (see experimental section). Substances (I) are quite resistant to dilute aqueous solutions of alkalies. A benzene solution of (VI) or (VII) was shaken constantly for three days with 0.5 N solution of sodium hydroxide after which the reaction mixture stood for two weeks longer. After this treatment (VI) and (VII) were recovered unchanged. On boiling (VI), which

had been reduced to a fine powder, with 2N aqueous solution of sodium hydroxide the reaction of hydrolysis does proceed but does so very slowly. The stability of (I) to aqueous solutions of alkalies is evidently mainly explained by their insolubility in water. On boiling substances (I) with 2N aqueous solution of alkalies diluted with two parts of alcohol, the hydrolysis reaction is completed within 20-40 minutes according to the scheme:

$$SO_2[N{=}P(OAr)_3]_2 \xrightarrow{+4NaOH} 2NaOAr + 2H_2O + SO_2[NNaPO(OAr)_2]_2 \longrightarrow$$
$$\xrightarrow{+2HCl} 2NaCl + SO_2[NHPO(OAr)_2]_2$$

In some cases better results are obtained by hydrolysis with alkalies in pyridine-alcohol solution (see experimental part).

Substances (XIV) of the type $SO_2[NHPO(OAr)_2]_2$ with Ar: C_6H_5 (XV), o-, m- and p-$CH_3C_6H_4$ (XVI), XVII and XVIII), α- and β-$C_{10}H_7$ (XIX and XX), p-ClC_6H_4 (XXI) and p-$O_2NC_6H_4$ (XXII), were synthesized by the scheme shown above. All the (XIV) thus prepared were microcrystalline substances which melted with decomposition and were insoluble or were but sparingly soluble in water; they were soluble in acetone, alcohol, dioxane, and chloroform. They were insoluble, even on heating, in nonpolar organic solvents: benzene, ether, carbon tetrachloride, petroleum ether and dichloroethane; they displace carbon acid from its salts and titrate with two equivalents of aqueous alkalies (with phenolphthalein). In contrast to diesters of arylsulfonamidophosphoric acids, substances (XIV) are rather readily cleaved at the nitrogen to sulfur bond on being boiled with water and especially readily in aqueous alcohol and alcoholic solutions. This fact is explained by the fact that (XIV) are derivatives of sulfamide which is readily hydrolyzed by water, alkalies and acids, while diesters of arylsulfonamidophosphoric acids are derivatives of arylsulfonamides which saponify only extremely difficultly (compare above). Properties of (XV) were studied in most detail, this substance being obtained in the form of finely crystalline snow-white powder with m.p. 185-187° (with decomposition) after reprecipitation with hydrochloric acid from an alkaline solution. It was impossible to recrystallize any significant amounts of (XV) from either water or alcohol (see above). Only a very small amount may be recrystallized from water (see experimental section). The melting point of (XV), recrystallized from water, is 188-189° (with decomposition). On being boiled with 96% alcohol the substance undergoes a cleavage of the sulfur–nitrogen bond and forms the diphenyl ester of amidophosphoric acid (XXV), which was identified by mixed melting point with authentic (XXV) [4], and a mixture of acidic uncrystallizable substances which are readily soluble in water, which were evidently sulfamic acid and diphenyl phosphate

$$[(C_6H_5O)_2PONH]_2SO_2 \xrightarrow{+2H_2O} (C_6H_5O)_2PONH_2 + NH_2SO_2OH + (C_6H_5O)_2POOH$$

Substances (XV) form readily crystallizable salts with alkalies: there were prepared sodium, potassium and ammonium salts (see the experimental section).

In their physical and chemical properties (XVI-XVIII) are rather similar to (XV) but in contrast with salts of (XV), the salts of (XVI-XVIII) precipitate from hot aqueous solutions on cooling in the form of an oil which is saturated with water. After being dried in a vacuum desiccator over sulfuric acid these salts gradually lose the water contained in them and are transformed into a hard glassy mass.

We failed to prepare (XIX) by hydrolysis of (IX) with aqueous alcoholic and alcoholic alkali in any satisfactory yield. After many hours of refluxing of the reaction mixture the yield of (XIX) was about 4%. We succeeded in carrying out the hydrolysis of (IX) with good yield in pyridine-alcohol solution (see experimental section).

Substance (XXI) has an interesting peculiarity: when dry it is absolutely in ether, but after being moistened with water it dissolves in ether quite easily. For other properties and peculiarities of (XIV) see the experimental section.

EXPERIMENTAL

The success of the synthesis of bis-triaryloxyphosphazo-sulfones depends to a considerable degree on the quality of the sodium arylates used for the reaction; these must be finely powdered, thoroughly dried and be quite pure. Thus, for example, after using some insufficiently pure sodium cresolates it was impossible to isolate

crystalline forms of (VII) and (VIII). The concentrated aqueous solutions of sodium arylates must be completely colorless or only slightly colored. Solutions of cresolates oxidize especially easily in the presence of excess of the cresols; such solutions darken in the presence of air very rapidly indeed even at room temperature. Therefore, sodium cresolates should be prepared by addition of cresols to precisely equivalent amounts of 20-25% solutions of sodium hydroxide, and not in reverse. The solutions of sodium cresolates should be evaporated in vacuum without a capillary or in a stream of an inert gas, at the temperature of a boiling water bath, with a subsequent drying at 150-180° over 2-3 hours. Both during the evaporation and during drying, right up to final cooling, no contact of the solutions or the solid sodium cresolates with atmospheric oxygen can be permitted. Pure dry cresolates are oxidized by atmospheric oxygen very slowly, but they must be meticulously protected from the action of moisture and carbon dioxide from the atmosphere, since the cresolates are easily oxidized in the presence of these substances.

The products of oxidation of the p-chlorophenolate are not colored, in contrast to the products of oxidation of sodium cresolates. Therefore, the color of the p-chlorophenolate is not a criterion of its purity. A known, spoiled p-chlorophenolate may be completely colorless. The p-chlorophenolate is oxidized by atmospheric oxygen particularly readily in the presence of free p-chlorophenol. In the synthesis of the p-chlorophenolate one may use a slight excess of the alkali, from which the product is easily separated by solution in ether with a subsequent distillation of the solvent in vacuum. About 11 g of sodium p-chlorophenolates dissolves in 100 g of ether. The p-chlorophenolate must be dried in vacuum at a temperature not under 150° and air should be admitted into the flask (nitrogen is better) only after complete cooling. Pure sodium p-chlorophenolate is completely soluble in ether.

Using sodium naphtholates, prepared by the usual method from the naphthols and aqueous solution of sodium hydroxide, it is impossible to prepare in a satisfactory yield the colorless crystalline specimens of (IX) and (X), since sodium naphtholates, either in dry state or in aqueous or ethereal solutions, are extremely easily oxidized by oxygen of the air. Therefore sodium naphtholates must be prepared from naphthols and metallic sodium in ethereal solutions in special apparatus which completely prevents any contact of the ethereal solutions of the naphtholates with oxygen in the air. The reaction of sodium naphtholates with bis-trichlorophosphazo-sulfone was run in the same apparatus in an atmosphere of hydrogen. The preparation and drying of the p-nitrophenolate does not present any difficulties.

All solvents used for the synthesis and the recrystallization of bis-triaryloxyphosphazo-sulfones must be pure and thoroughly dehydrated. All operations must be run in such a manner that the starting materials and the reaction mixtures come in contact with atmospheric moisture as little as possible.

Bis-triphenoxyphosphazo-sulfone (V). To a solution of 0.05 mole of bis-trichlorophosphazo-sulfone (XIII) in 200 ml of benzene there was added at once with energetic stirring 0.31 mole of sodium phenolate which operation causes a vigorous boiling of the mixture. After the cessation of the spontaneous boiling, the mixture was refluxed for thirty minutes on a water bath. The precipitate of sodium phenoxide disappears and there is formed a slimy precipitate of sodium chloride. If the starting materials were pure, the mixture remains quite colorless. The benzene is removed completely in vacuum, finally on a boiling water bath, and 50.0 ml of water is added to the residue, whereupon (V) precipitates in the form of a colorless finely crystalline precipitate. The product is filtered off by suction (the filtrate should be neutral or slightly alkaline but never acidic), washed with water and dried over sulfuric acid in vacuum; yield is 95-98%, m.p. 131-132°. In case the product is obtained in a colored state (this takes place after use of insufficiently pure sodium phenolate) it is washed several times with alcohol, which somewhat reduces the yield. After recrystallization from benzene (16.4 g from 200 ml) there is formed 12.2 g of (V) in the form of colorless flat rectangular prisms with m.p. 132-133°. The substance is insoluble in water and cold petroleum ether; it is soluble with difficulty in boiling petroleum ether, and is readily soluble in boiling alcohol, benzene, carbon tetrachloride, acetone and chloroform, and difficultly soluble in these solvents in the cold. About hydrolysis of (V) see below.

Found %: C 60.43; H 4.19; N 3.77, 3.88; S 4.45; P 8.75. M 695, 705. $C_{36}H_{30}O_8N_2SP_2$. Calculated %: C 60.64; H 4.21; N 3.93; S 4.50; P 8.71. M 712.4.

Bis-tri-o-cresoxyphosphazo-sulfone (VI) was prepared similarly to (V); yield 93-95%. Soluble in all organic solvents considerably more readily than (V). Crystallizes from benzene with one molecule of benzene, the crystallohydrate having m.p. 105-115°.

Found %: C_6H_6 9.22. $C_{42}H_{42}O_8N_2SP_2 \cdot C_6H_6$. Calculated %: C_6H_6 9.81.

The crystallohydrate with benzene is easily "weathered" in air or by washing with ether. After drying in vacuum at 100° or crystallization from ether there is obtained (VII) which does not contain the benzene of crystallization; m.p. 127-129°.

Found %: N 3.42, 3.34. $C_{42}H_{42}O_8N_2SP_2$. Calculated %: N 3.52.

Bis-tri-m-cresoxyphosphazo-sulfone (VII). The synthesis was run as was that of (V). After distillation of benzene in vacuum there remained a viscous uncrystallizing mixture of sodium chloride and (VII) to which there was added 200-250 ml of ether (free of peroxides) and 100 ml of water and the mixture was shaken energetically. After separation of the aqueous layer, the ethereal layer was washed with N solution of sodium hydroxide and several times with 10-15% solution of sodium chloride. If the ethereal layer remained cloudy, it was finally washed with a saturated solution of sodium chloride. The ethereal solution was washed as above, then dried with sodium sulfate, after which the ether was distilled, finally in vacuum. The residue was crude (VII) in the form of a viscous almost colorless slowly crystallizing oil. The composition of the crude (VII) in respect to nitrogen content did not differ from that of pure crystalline substance; the yield was about 90%. For preparation of the crystalline substance, there was added to crude (VII) such a volume of ether so as to bring the entire mass into solution on heating, after which the solution was filtered if needed, and was treated with petroleum ether (85-95°) in the amount needed to cause cloudiness. A crystalline seed was added to the solution and this was allowed to stand for one day at room temperature. Large well formed prismatic crystals of (VII) precipitated from the solution; yield was about 40%; m.p. 54-56°.

Found %: N 3.52. $C_{42}H_{42}O_8N_2SP_2$. Calculated %: N 3.52.

Bis-tri-p-cresoxyphosphazo-sulfone (VIII) was prepared just like (VII), but crystallized much more readily. The yield of crude (VIII) in the form of oil was 88.0%; the yield of crystalline (VIII) was 62.0%; m.p. 80-81°. The compositions of the crude and the crystalline (VIII) in respect to nitrogen content were identical.

Found %: N 3.60. $C_{42}H_{42}O_8N_2SP_2$. Calculated %: N 3.52.

Bis-tri-α-naphthoxyphosphazo-sulfone (IX). The preparation of sodium α-naphtholate, filtration of its solution, its mixing with the solution of (XIII) and the addition of dilute hydrochloric acid to the reaction mixture were all performed in nitrogen atmosphere or hydrogen atmosphere in a special apparatus which permitted the complete prevention of contact by the solutions with atmospheric oxygen. The construction of the apparatus is not described here since it is rather complicated, but this has no fundamental significance. Any apparatus may be suitable as long as it permits one to run the reaction in the absence of atmospheric oxygen.

The filtered solution of 0.066 mole of α-naphthol in 30.0 ml of ether was poured into the flask containing 0.09 gram atoms of sodium in the form of a thin wire (or cut into thin slices) and 25.0 ml of ether. A vigorous reaction began immediately, the solution first turning blue, then soon becoming almost colorless. If necessary, the flask was cooled with cold water. One should watch that the volume of the solution never drops below 45-50 ml owing to the loss of ether by the evolving hydrogen, and one should add small volumes of ether from time to time since the omission of this may result in solid naphtholate depositing on the surface of sodium and thus causing the reaction to stop. After the reaction had been completed, the naphtholate solution was filtered from excess sodium, heated to 30° and added slowly with energetic stirring to the solution of 0.01 mole of (XIII) in 50.0 ml of ether at such a rate as to cause the reaction mixture to boil vigorously. A snow white precipitate forms during this operation, this being a mixture of sodium chloride and (IX). After the vigorous reaction had been completed, the reaction mixture was refluxed for 15-20 minutes on a water bath, then cooled and slowly treated with stirring with 15.0 ml of N hydrochloric acid. The ethereal and the aqueous layers separate rapidly, both being transparent. All further operations were done conventionally. (IX)is present in the aqueous layer in the form of finely crystalline powder which was filtered off, washed thoroughly with ether and water and then dried in air. (IX) prepared in this manner is a completely colorless finely crystalline powder; the yield is 90-95%, after recrystallization from chlorobenzene (5.0 g per 30.0 ml) m.p. 205-206°. If air enters the apparatus during the synthesis prior to the addition of hydrochloric acid, (IX) is obtained in a colored state – from light grey to black. The substance is readily soluble in acetone, difficultly soluble in most of the common organic solvents and insoluble in water.

Found %: N 2.77. $C_{60}H_{42}O_8N_2SP_2$. Calculated %: N 2.76.

Bis-tri-β-naphthoxyphosphazo-sulfone (X) was prepared just like (IX); the yield was 74-79%. For recrystallization, 15.0 g of the product was dissolved in 80.0 ml of acetone; the solution was filtered and somewhat over half of the acetone was distilled off; to the residual solution was added about 100 ml of ether (until cloudiness formed). After one day the precipitated crystals were filtered off by suction and washed with ether; m.p. 133-134°. (X) is readily soluble in acetone, insoluble in water and difficultly soluble in the majority of common organic solvents.

Found %: N 2.85. $C_{60}H_{42}O_8N_2SP_2$. Calculated %: N 2.76.

Bis-tri-p-chlorophenoxyphosphazo-sulfone (XI). To the solution of 0.01 mole of (XIII) in 50.0 ml of ether there was added at once the solution of 0.063 mole of sodium p-chlorophenolate (see above for the preparation of the arylates of sodium) in 100 ml of ether. After the vigorous reaction had subsided (boiling-up, formation of the precipitate), the mixture was refluxed for 20 minutes. Then ether was distilled off in vacuum and 20.0 ml of water was added to the residue. If the starting materials were quite pure, (XI) precipitates in a crystalline form or in the form of an oil which rapidly crystallizes. The product was filtered off, washed with water, 0.2 N solution of sodium hydroxide, then again with water and then dried. The yield was 80-85%. For purification the product was dissolved in 15.0 ml of boiling benzene and then treated with 20-30 ml of petroleum ether. (XI)precipitated from the solution in the form of fine colorless prisms, m.p. 111-113°. It is readily soluble in acetone, difficultly in ether and benzene.

Found %: N 3.16. $C_{36}H_{24}O_8N_2Cl_6SP_2$. Calculated %: N 3.05.

Synthesis of (XI)may be carried out in benzene with dry sodium p-chlorophenolate but the yield in this case is considerably lower. In some cases during the synthesis of (XI) with insufficiently pure dry sodium p-chlorophenolate there were obtained large colorless prisms with m.p. 85-86°, which after recrystallization from ether were converted into pure (XI) with m.p. 111-113°. The mixed melting point of these prisms with (XI) melted at 68-110°. Evidently the substance with m.p. 85-86° was a double complex of (XI) with p-chlorophenol. This substance was not examined in more detail.

Bis-tri-p-nitrophenoxyphosphazo-sulfone (XII). To 0.062 mole of dry powdered sodium p-nitrophenolate there was added with stirring the solution of 0.01 mole (XIII) in 30.0 ml of nitrobenzene. The mixture heated up considerably but failed to boil. After termination of this reaction, the mixture was heated on an oil bath until the p-nitrophenolate dissolved (120-125°). Sodium chloride precipitated on cooling and (XII) began to crystallize in small shiny prisms. To the still warm mixture there was added 50.0 ml of ether, the whole being well stirred, then allowed to stand for two hours, treated with 30.0 ml of water, again stirred vigorously, after which (XII)was filtered off, washed thoroughly with water, then with acetone (twice with 15.0 ml) and ether (three times with 20.0 ml). The yield was 80%. For purification the substance was dissolved in nitrobenzene preheated almost to boiling (1.0 g for 2.0 ml), the solution was immediately filtered while hot, and treated with 5 volumes of acetone. After a few minutes (XII) began to precipitate in the form of small shiny prisms. After one hour the product was filtered off, washed with acetone (five times with 10.0 ml) and ether (four times with 10.0 ml). The yield was 53%; m.p. 198-200°, with sintering noted at 195°.

Found %: N 11.67. $C_{36}H_{24}O_{20}N_8SP_2$. Calculated %: N 11.40.

(XII) may also be prepared in a benzene solution but the yields in this case are low, the reaction must be run for several hours and the isolation of a pure product is complicated by considerable difficulties [see preparation of (V)]. The substance is insoluble in water and the usual organic solvents. It is readily soluble in hot pyridine and nitrobenzene. It decomposes rather rapidly in boiling nitrobenzene solutions.

Tetraphenyl ester of N,N'-sulfamidobisphosphoric acid (XV). To 60.0 ml of 2 N aqueous solution of sodium hydroxide there was added 70.0 ml of alcohol and 0.031 mole of thoroughly powdered (V). The mixture was refluxed with stirring until the precipitate dissolved almost completely, which required about 20 minutes. The solution was filtered and concentrated in vacuum to half the original volume and the residue was treated with a mixture of 25.0 ml of 5 N hydrochloric acid and 20.0 ml of alcohol. Thereby (XV) precipitated in the form of a colorless cheesy mass. The product was filtered off, washed with water and dried in air. The yield was 92.0%. For purification the substance was dissolved in 2 N aqueous alcoholic solution of sodium carbonate and this solution was poured into an aqueous alcoholic solution of 3 N hydrochloric acid. The (XV) prepared in this manner was a colorless finely crystalline powder, m.p. 185-187° (decomposition). On being boiled with water and alcohol the substance decomposes rather rapidly but small amounts of it may be recrystallized from water. To do this one

adds 1.0 g of finely powdered (XV) to 300 ml of boiling water, the mixture being shaken vigorously and filtered immediately. On cooling the solution precipitates (XV) in the form of fine shiny needles with m.p. 188-189° (decomposition). See above about the solubility of (XV).

Found %: N 4.83, 4.86. Equivalents 2.01, 2.00. $C_{24}H_{22}O_8N_2SP_2$. Calculated %: N 5.00. Equivalents 2.00.

Cleavage of (XV) on boiling with alcohol. A mixture of 0.01 mole of (XV) and 40.0 ml of 96% ethyl alcohol was refluxed for thirty minutes after which the alcohol was distilled off in vacuum from a water bath. On cooling a crystalline diphenyl ester of amidophosphoric acid (XXV) precipitated, this being filtered off and washed with alcohol (three times with 1.0 ml); m.p. 148-149°; yield 0.0075 mole; the identification was done by mixed melting point with authentic (XXV) [4]. Substances which remained in solution gave an acid reaction with Congo red and decomposed sodium bicarbonate. From 0.01 mole of (XV) there was formed 0.0081 mole of (XXV) and a mobile colorless oil with an acid reaction to Congo red, after an analogous experiment with anhydrous methyl alcohol. Triaryloxyphosphazosulfonophenyls are unchanged even after prolonged boiling with alcohol.

Sodium salt of (XV). (XV) (0.004 mole) was mixed with 5.0 ml of water and 0.004 mole of sodium carbonate. The substance dissolved with hissing. The sodium salt of (XV) precipitated in the form of well developed elongated prisms which were filtered off and washed with a small volume of water. The yield was about 2.2 g; m.p. 44-57°. The salt contains ten molecules of water of crystallization, a considerable part of which is easily lost by simple storage in air, which fact explains the extended melting range.

Found %: H_2O 25.05. $C_{24}H_{20}O_8N_2SP_2Na_2 \cdot 10H_2O$. Calculated %: H_2O 24.69.

The hydrate is completely dehydrated after storage in vacuum over sulfuric acid. The anhydrous salt melts at 252-254° (with decomposition).

Found %: N 4.57. $C_{24}H_{20}O_8N_2SP_2Na_2$. Calculated %: N 4.65.

Decomposition evidently precedes the melting of the anhydrous salt since the salt heated in vacuum above 100° no longer dissolves completely in water and does not regenerate the hydrate on being treated with water, while the salt which had been dried in vacuum over sulfuric acid at room temperature is completely soluble in water and readily regenerates the hydrate with ten molecules of water.

Potassium salt of (XV) was prepared analogously to the sodium salt. The hydrate of the potassium salt contains seven molecules of water of crystallization and melts at 52-54°; it loses water somewhat less readily than does the hydrate of the sodium salt, but it still weathers on being stored in air.

Found %: H_2O 15.90. $C_{24}H_{20}O_8N_2SP_2K_2 \cdot 7H_2O$. Calculated %: H_2O 16.53.

The hydrate loses water completely in vacuum at 40-50°.

Found %: N 4.46. $C_{24}H_{20}O_8N_2SP_2K_2$. Calculated %: N 4.40.

Ammonium salt of (XV). (XV) (0.002 mole) was dissolved with mild heating in 2.0 ml of concentrated aqueous solution of ammonia. Small colorless crystals of the ammonium salt precipitated on cooling; yield was 1.22 g; m.p. 63-67°. The salt contained four molecules of water of crystallization which were not weathered off in storage in air.

Found %: H_2O 10.92. $C_{24}H_{28}O_8N_4SP_2 \cdot 4H_2O$. Calculated %: H_2O 10.81.

The hydrate loses water completely in vacuum at 100°.

Found %: N 8.45. $C_{24}H_{28}O_8N_4SP_2$. Calculated %: N 8.45.

Tetra-o-tolyl ester of sulfamidobisphosphoric acid (XVI) was prepared just like (XV). Yield was 80%; m.p. 173-176° (with decomposition).

Found %: N 4.37. Equivalents 1.97. $C_{28}H_{30}O_8N_2SP_2$. Calculated %: N 4.55. Equivalents 2.00.

Tetra-m-tolyl ester of sulfamidobisphosphoric acid (XVII) was prepared just like (XV) but refluxing was continued for one hour since (VII) hydrolyzes considerably more slowly than does (V). The yield was 73%; m.p. 170-172° (with decomposition).

Found %: N 4.56. Equivalents 2.00. $C_{28}H_{30}O_8N_2SP_2$. Calculated %: N 4.55. Equivalents 2.00.

Tetra-p-tolyl ester of sulfamidobisphosphoric acid (XVIII) was prepared just like (XVII). Yield was 87%; m.p. 184-185° (with decomposition).

Found %: N 4.36. Equivalents 2.00. $C_{28}H_{30}O_8N_2SP_2$. Calculated %: N 4.55. Equivalents 2.00.

Tetra-α-naphthyl ester of sulfamidobisphosphoric acid (XIX). To 16.0 ml of N alcoholic solution of potassium hydroxide there was added a hot solution of 0.004 mole (IX) in 10.0 ml pyridine and the mixture was refluxed. It was impossible to determine the end of the reaction by dilution of a sample with water since the potassium salt of (XIX) is very difficultly soluble in water and precipitates on dilution along with unreacted (IX). Under the above conditions the hydrolysis is completed during 1-1.5 hours. The solution was filtered while hot and to the filtrate there was added with stirring 15.0 ml of concentrated hydrochloric acid. (IX) was filtered off after one day; it was washed thoroughly with water then with ether. The yield was 92%. For purification (XIX) was dissolved in 0.3 N alcoholic potassium hydroxide and the hot solution was treated with hydrochloric acid. (XIX) precipitated on cooling in the form of small shiny crystals; m.p. 213-215° (with decomposition).

Found %: N 3.78. Equivalents 2.02. $C_{40}H_{30}O_8N_2SP_2$. Calculated %: N 3.68. Equivalents 2.00.

(XIX) decomposes considerably more slowly than does (XV)-(XVIII) on being boiled in aqueous alcoholic solutions. Sodium salt of (XIX) is more difficultly soluble in water and for this reason the titrations are run in hot aqueous alcoholic solution.

Tetra-β-naphthyl ester of sulfamidobisphosphoric acid (XX). A mixture of 0.004 mole of finely powdered (X), 8.2 ml of 2 N potassium hydroxide and 25.0 ml of alcohol were refluxed until the substance had dissolved completely (30-40 minutes), when a mixture of 5.0 ml of 5 N hydrochloric acid and 5.0 ml of alcohol was added. (XX) was filtered off after several hours and was thoroughly washed with water and ether to remove traces of naphthol. The yield was 94%. From dilute hot aqueous alcoholic solution one may precipitate (XX) by acidification; it forms fine shiny prisms; m.p. 195-198° (with decomposition). (XX) is titrated just like (XIX).

Found %: N 3.70. Equivalents 1.97, 2.01. $C_{40}H_{30}O_8N_2SP_2$. Calculated %: N 3.68. Equivalents 2.00.

Tetra-p-chlorophenyl ester of sulfamidobisphosphoric acid (XXI). A mixture of 0.002 mole (XI), 4.0 ml of 2 N potassium hydroxide and 8.0 ml of alcohol were refluxed until the substance dissolved completely (10-15 minutes), after which there was added 2.0 ml of 5 N hydrochloric acid. The solution at first turned cloudy and after several minutes there began to precipitate the thread-like crystals. (XXI) was filtered off after one day and was washed with water. The yield was 79%; m.p. 183-185° (with decomposition).

Found %: N 4.03. Equivalents 2.01. $C_{24}H_{18}O_8N_2Cl_4SP_2$. Calculated %: N 4.02. Equivalents 2.00.

Tetra-p-nitrophenyl ester of sulfamidobisphosphoric acid (XXII). (XII) (0.02 mole) was refluxed with 8.0 ml of N alcoholic solution of potassium hydroxide and 17.0 ml of alcohol until the precipitate was completely dissolved (30-40 minutes). The cloudy yellow solution was filtered hot and after cooling was treated with 5.0 ml of 2 N hydrochloric acid. (XXII) precipitated in the form of a very fine crystalline powder which was filtered off and washed with a large volume of water, followed by ether. The yield was about 30%. Salts of (XXII) are very difficultly soluble in water and alcohol, which fact complicates the purification of (XXII). The substance decomposes rapidly on being heated in alcoholic or aqueous solutions. It is best to reprecipitate (XXII) from hot solutions in 0.1 N alcoholic potassium hydroxide. The reprecipitated (XXII) forms a finely crystalline powder; m.p. 218-221°.

Found %: N 11.38. $C_{24}H_{18}O_{16}N_6SP_2$. Calculated %: N 11.35.

SUMMARY

The reaction of bis-trichlorophosphazo-sulfone with sodium arylates was studied and bis-triaryloxyphosphazo-sulfones were prepared.

The hydrolysis of bis-triaryloxyphosphazo-sulfones was studied and tetraaryl esters of sulfamidobisphosphoric acid were prepared.

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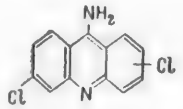
CHEMICAL STRUCTURE AND PARASITOCIDAL ACTIVITY

XXI. CONCERNING THE PROBLEM OF THE CONNECTION OF THE STRUCTURAL STABILITY OF DERIVATIVES OF 9-AMINOACRIDINE AND THEIR ANTIMALARIAL ACTION

A. F. Bekhli

The acridine nucleus and the dialkylaminoalkylamine side chain in 9-position are the basic structural elements of the most important group of antimalarial compounds – derivatives of 9-aminoacridine. Various points of view have been expressed about the mechanism of action of these compounds against the plasmodiae. On one hand, attempts were made to explain the activity by the action of the products of decomposition of derivatives of 9-aminoacridine on the parasite [1]; on the other hand, the activity was explained by the action of the whole, intact molecule [2-4]. We set for our goal the study of the dependence of antimalarial action on the stability of the fundamental structure of the molecule, i.e., on the relative stability of the link of the side chain with the acridine nucleus. It was established by biological tests in the groups of monochloro- and dichloro isomers of 9-dialkylamino-alkylaminoacridine [5, 6] synthesized by us, that the degree of the antimalarial activity is connected with the position of the halogen in the acridine nucleus. The determination of the rate of hydrolytic cleavage of ammonia from the group of monochloro isomers of 9-aminoacridine, performed by us [7], showed that the largest amount of ammonia is cleaved from 4-chloro-9-aminoacridine, whose dialkylaminoalkyl analog is inactive against malaria. Conversely, a considerable structural stability under hydrolytic conditions was shown by 1- and 3-chloro derivatives of 9-aminoacridine, whose 9-dialkylaminoalkyl analogs were the most effective agents against malaria.

The purpose of the present work is the further study of the dependence of the antimalarial activity on the hydrolyzability in the series of dichloro derivatives of acridine. In view of the fact that 9-aminoacridines are close to N-monosubstituted derivatives of 9-aminoacridines [8] in their chemical and physical properties and considering that the hydrolysis of 9-aminoacridines may be controlled more readily, we took for our study in this case, as well, the analogs of dichloro isomers of 9-dialkylaminoalkylaminoacridines which did not contain alkyl groups, for the study of the rate of hydrolysis of these substances. For this we synthesized 1,6-, 2,6-, 3,6-, and 4,6-dichloro derivatives of 9-aminoacridine and subjected them to alkaline hydrolysis. These compounds were prepared by condensation of the corresponding 9-phenoxy compounds with ammonium chloride [9] or of the corresponding 9-chloro derivatives with ammonium carbonate [10] in phenol. The hydrolysis was run in a basic solution with titration of the evolved ammonia by the method which has been described previously by us [7]. At the same time we showed that the rate of hydrolysis was the same in acidic and basic media. The results of the hydrolysis are shown in Table 2.



The data secured by us indicate that the least stable, under the conditions of the hydrolysis, is 4,6-dichloro-9-aminoacridine, whose dialkylaminoalkyl analog turned out to be completely inactive against malaria. The other isomers possess greater stability to hydrolytic cleavage, losing a smaller amount of ammonia. At the same time it was found that their dialkylaminoalkyl analogs possess antimalarial activity.

It should be mentioned that the technique used by us brings out in this group of compounds only the basic character of the dependence of the relative stability of the molecule to hydrolysis, their antimalarial activity and the position of the halogen. This dependence shows that one of the necessary conditions for antimalarial activity

TABLE 1

Dichloro-9-aminoacridines

Position of chlorine atoms	Method	Melting point*	Yield (in %)	Found N** (in %)
1,6-	B	265—266°	40	10.33, 10.76
2,6-	B	299—300	40	10.61, 10.56
3,6-	B	293—294	37.9	10.73, 10.48
4,6-	A	271—272	91.2	10.57, 10.79

*The compounds were crystallized from alcohol.

**$C_{13}H_8N_2Cl_2$. Calculated %: N 10.65.

TABLE 2

Position of chlorine atoms in dichloro-9-aminoacridine	Sample (in g)	Amount of 0.01 N HCl consumed in neutralization of ammonia distilled with 100, 150 and 200 ml of water		
		100	150	200
1,6-	0.1020	6.8	7.9	9.0
	0.1018	6.4	7.2	8.0
	0.1019	6.5	7.7	8.4
2,6-	0.1018	4.6	5.4	6.4
	0.1018	5.2	6.3	7.2
	0.1019	4.3	5.0	5.5
3,6-	0.1018	6.3	7.2	7.9
	0.1020	6.9	7.8	8.8
	0.1018	6.3	7.7	8.8
4,6-	0.1027	9.0	11.0	12.5
	0.1018	8.0	10.1	11.4
	0.1018	8.0	9.4	10.9

in this group of compounds is the structural stability of the molecule. Thus, with a few and thus far unexplained exceptions (for example: 2,6-dichloro-9-aminoacridine), the considerable resistance to hydrolytic cleavage is observed in the most active compounds of the series. The establishment of more precise interrelationships between hydrolyzability and antimalarial activity of the compounds is hindered by the insufficient accuracy of the analytical methods used and possible variations of the results of the biological tests. The above conclusion finds some confirmation in the examination of some experimental data obtained by other investigators.

We compared the data on the determination of the rate of hydrolysis among atebrin homologs with various lengths of the side chain [11], with their antimalarial activity found by other investigators [12]. This contraposition showed that the rate of hydrolysis decreases with the increase of antimalarial activity in the groups of 9-dialkylaminoalkylacridines themselves. The synthesized 2-methoxy-6-chloro-7-amino-9(δ-diethylamino-α-methylbutyl)aminoacridine [13-15] and some of its analogs, which have high chemotherapeutic indexes than does acriquine show at the same time a greater stability than the latter on being boiled with water and in a weakly acidic solution. Finally we should note the facile hydrolyzability of the acridine derivatives with a tertiary nitrogen atom in 9-position [1, 16, 17] and should compare it with the absence of any antimalarial effectiveness of such compounds, as for example the N-formyl derivative of atebrin [18].

Thus, this group of compounds also confirms that the derivatives of 9-aminoacridine which are ineffective against malaria are simultaneously unstable to hydrolysis. At the same time, compounds which are stable under the conditions of hydrolysis show a high antimalarial activity. Regardless of the factors which may affect the stability of the link of the acridine nucleus with the side chain, the presence of such a stability is one of the conditions for antimalarial activity of derivatives of 9-aminoacridine.

EXPERIMENTAL

Dichloro-9-aminoacridines were prepared by the method of Drozdov [9] (method A) by condensation of 9-phenoxy derivatives of acridine with ammonium chloride in phenol, and by the method of Albert [10] (method B) by the reaction of appropriate derivatives of 9-chloroacridine with ammonium carbonate, in phenol. The substances prepared by us are given in Table 1.

The determination of the relative rates of hydrolysis of dichloro-9-aminoacridines was performed by the method described by us previously [7] for the hydrolysis of monochloro-9-aminoacridines in a basic medium with absorption of the ammonia. The experimental conditions were the same for all the compounds studied. The results which were secured are shown in Table 2.

SUMMARY

1. Isomeric 1,6-, 2,6-, 3,6-, and 4,6-dichloro-9-aminoacridines were synthesized.

2. The relative rates of hydrolysis of the synthesized isomeric dichloro-9-aminoacridines were determined by their being boiled in a basic medium. It was found that the compounds being studied lost ammonia at different rates; the greatest rate of decomposition was discovered in 4,6-dichloro isomer.

3. The closeness of the chemical properties of the dichloro-9-aminoacridines studied by us to those of the corresponding dichloro-9-dialkylaminoalkylaminoacridines permits us to characterize the relative stability of the link of the nucleus with the side chain among the latter group of compounds, on the basis of the data secured about the hydrolysis of the former group. The results which were obtained showed, in comparison with the data from other authors, that the antimalarial action of the dichloro derivatives of 9-dialkylaminoalkylaminoacridine is possible only under the condition of a sufficient stability of these compounds to hydrolytic decomposition; this gives us the basis to regard the antimalarial action as being manifested by the intact unchanged molecule.

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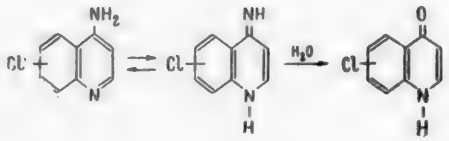
CHEMICAL STRUCTURE AND PARASITOCIDAL ACTIVITY

XXII. CONCERNING THE PROBLEM OF THE CONNECTION BETWEEN THE STRUCTURE AND THE ANTIMALARIAL ACTION OF ISOMERIC CHLORO-4-AMINOQUINOLINES

A. F. Bekhli

A number of investigators [1-5] were occupied by the study of the connection between the structure and the antimalarial activity of the derivatives of 4-aminoquinoline. Chloroquine, 7-chloro-4(δ -diethylamino-α-methylbutyl)aminoquinoline, a representative of the derivatives of 4-aminoquinoline which possesses a high antimalarial activity, has been subjected to an all-inclusive study. It turned out that chloroquine does not suffer any changes after being heated to 100° in an acid medium [6], being a stable compound. Studies of the metabolism of the highly effective derivatives of 4-aminoquinoline showed that these substances are eliminated from the organism in an unchanged state, preserving the structure of their molecule [7]. Taylor and co-workers [8] found that chloroquine has antimalarial activity in vitro, i.e., under conditions which exclude an alteration of its molecule. Isomers of chloroquine which contain chlorine in positions 5, 6 or 8 showed a weak antimalarial effectiveness or its total absence in appropriate biological tests [4]. Therefore the chloro derivatives of 4-dialkylaminoalkylaminoquinoline, as well as the chloro derivatives of 9-aminoacridine [9] display a different level of antimalarial activity depending on the position of the halogen in the benzenoid part of the quinoline nucleus.

We attempted to determine whether or not the rate of hydrolytic cleavage of the amino group depends on the position of the halogen and, consequently, whether or not a connection exists between the hydrolyzability and the antimalarial activity of the derivatives of 4-aminoquinoline. An analogous problem was studied by us previously [10] with the derivatives of 9-aminoacridine and a first attempt was made to explain the different activity of the individual chlorodialkylaminoalkyl derivatives of that group by the relative stability of the link of the 9-amino group with the acridine nucleus, depending on the position of the halogen. The study of the relative rates of hydrolysis could be run, as it appeared to us, not on 4-dialkylamino derivatives of quinoline themselves but on the corresponding 4-aminoquinolines. The latter are a convenient model owing to the fact that in hydrolysis they lose ammonia, which is readily captured and may be titrated with an acid in the presence of an indicator.



For the accomplishment of the problem before us it was necessary to have 5-, 6-, 7- and 8-chloro-4-aminoquinolines; the 5-, 6- and 8-chloro derivatives were synthesized from the corresponding derivatives of 4-chloroquinoline and ammonia in phenol at 170° [11]. The isomer with the chlorine in 7-position was prepared by the method of condensation of 7-chloro-1,2,3,4-tetrahydro-4-quinolone with ammonia, developed by us earlier [12]. The 5- and 8-chloro-4-aminoquinolines were synthesized by us for the first time. 6-Chloro-4-aminoquinoline has been prepared earlier by Naito [13] by another method and turned out to be identical with our product.

In the study of the relative stability of the amino group link to the quinoline nucleus, depending on the position of the halogen in the compounds being studied, samples of equal weights were boiled with a solution of

alkali. The liberated ammonia was steam distilled and determined by the usual analytical methods, by the technique which was used by us for the corresponding 9-aminoacridines [10].

The results obtained by us show that under the same conditions of hydrolysis the greatest stability is shown by 7-chloro-4-aminoquinoline, which loses the least amount of ammonia. As indicated above, its dialkylaminoalkyl derivative (chloroquine) is the most effective (Q = 15) of this important group of isomeric chloro-4-dialkylaminoalkylaminoquinolines [4]. 6-Chloro-4-aminoquinoline turns out to be less stable, losing more ammonia, than the 7-chloro isomer but less than 5- and 8-chloro isomers. Here it appeared that the effectiveness of 6-chloro-4-(δ-diethylamino-α-methylbutyl)aminoquinoline (Q = 2) is also considerably lower than the effectiveness of chloroquine and higher than the activity of the corresponding 5- and 8-chloro isomers (Q = 0.6 and 0.4).

The technique of hydrolysis used by us, as well as the possible fluctuations of the biological tests, cannot give a quantitative correlation of the biological activity of the compounds with their ability to be hydrolyzed. However on the basis of the results obtained by us one may consider that 7-chloro-4-aminoquinoline, which corresponds to the most active compound of this series and which loses the least amount of ammonia, is the most stable one under the conditions of hydrolysis. The great stability found in 7-chloro-4-aminoquinoline as well as the literature data cited above permit us to consider that chloroquine, in contrast to its poorly effective and more readily hydrolyzable isomers, displays its antimalarial action through preservation of its structure.

EXPERIMENTAL

The chloro derivatives of 4-aminoquinoline were prepared by two methods: A) condensation of derivatives of 4-chloroquinoline with ammonia in phenol medium [11] and B) condensation of derivatives of 1,2,3,4-tetrahydro-4-quinolone with ammonia in phenol [12]. The bases prepared by us were crystallized from benzene (Table 1) and their hydrochlorides gave a basic reaction to litmus.

TABLE 1

Chloro-4-aminoquinolines and Their Hydrochlorides

Position of the chlorine	Method of synthesis	Base			Hydrochloride		
		Yield (%)	Melting point	Found % of N**	Melting point	Found %***	
						N	Cl (ionic)
5-	A	98	120°	15.54, 15.56	309—310°	13.32, 13.12	
6-	A	97	233—234	15.65, 15.62	302—303	12.96	16.45, 16.47
7-	B	49	149.5—150*	—	291.5—292	13.00	16.60
8-	A	93.5	196—197	15.99, 15.91	287.5	13.01, 12.83	16.33, 16.37

*Literature data [11]: m.p. 151°.

**$C_9H_7N_2Cl$. Calculated %: N 15.69.

***$C_9H_8N_2Cl_2$. Calculated %: N 13.02, Cl (ionic) 16.49.

Determination of relative rates of hydrolysis of chloro derivatives of 4-aminoquinoline [10]. Into a wide mouthed flask with 1 liter capacity, provided with a liquid trap and a wide straight tube in its stopper, there was placed 300 ml of distilled water and a 45% solution of sodium hydroxide (72 ml). A sample of 0.1007 g of 7-chloro-4-aminoquinoline, wrapped in foil, was introduced into the boiling alkaline solution. The wide tube was immediately stoppered. The foil dissolved rapidly in the alkali and the substance mixed with the boiling liquid. Ammonia distilled along with water into a receiver containing distilled water acidified with a measured volume of 0.01 N hydrochloric acid, and containing a few drops of methyl orange; the distillation of ammonia was immediately noted by the color change in the indicator. The ammonia distillate was titrated with hydrochloric acid as it came over. The volume of 0.01 N hydrochloric acid needed to neutralize ammonia distilled with 100, 150 and 200 ml of water was noted. The results of hydrolysis are given in Table 2.

TABLE 2

Results of Determination of Relative Rates of Hydrolysis of Isomeric Chloro-4-Aminoquinolines

Position of chlorine	Sample (in g)	Ml of 0.01 N HCl used for neutralization of ammonia distilled with 100, 150 and 200 ml of water		
		100	150	200
5-	0.1003	5.2	8.4	14.0
	0.1021	5.5	8.3	12.3
	0.1001	5.2	7.8	12.4
6-	0.1000	4.0	4.8	5.9
	0.1027	4.2	4.9	6.1
	0.1009	4.0	4.9	5.9
7-	0.1007	3.3	3.9	4.8
	0.1010	3.2	4.2	5.2
	0.1009	3.0	3.8	4.9
8-	0.1011	4.8	5.7	6.9
	0.1004	4.8	5.8	6.9
	0.1001	5.0	5.8	6.8

SUMMARY

1. 5-, 6-, 7- and 8-chloro-4-aminoquinolines were synthesized. The relative rate of hydrolytic cleavage of ammonia in the compounds thus prepared was determined. It was found that under the conditions of hydrolysis used the greatest stability was shown by the 7-chloro isomer, which lost the smallest amount of ammonia.

2. The greatest stability of the link of the 4-amino group with the quinoline nucleus in the 7-chloro isomer, which was found in this work, in comparative reference to other isomeric compounds in this series, permits us to explain the high effectiveness of chloroquine, which is the diethylaminopentyl derivative of the indicated 7-chloro isomer, by the structural stability of its molecule under the conditions of hydrolytic decomposition.

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AN IMPROVED METHOD OF SYNTHESIS OF DI-β,β'-CHLOROETHYL ESTER OF β-CHLOROETHYLPHOSPHONIC ACID

E. L. Gefter

M. I. Kabachnik and P. A. Rossiiskaia [1] prepared di-β,β'-chloroethyl ester of β-chloroethylphosphonic acid by the Arbuzov isomerization of tris-β,β',β"-chloroethyl phosphite.

$$P(OCH_2CH_2Cl)_3 \xrightarrow{t^\circ} ClCH_2CH_2PO(OCH_2CH_2Cl)_2$$

However, the process of this isomerization presents a certain hazard to the experimenter since at above 150-160°, or in the presence of local spots of superheating, there begins an extremely violent reaction of an almost explosive type. The isomerization proceeds very slowly at below 150°. The yield of the isomerized product amounts to but 40% of the theoretical. The reason for this lies in the course of the reaction going simultaneously according to monomolecular (or bimolecular) and peculiar stepwise mechanisms. The latter leads to the formation of a considerable amount of undistillable sirup [2]. We succeeded in eliminating these defects from the process (the first one completely, the second in part), by running the isomerization of tris-β,β',β"-chloroethyl phosphite with energetic stirring in the presence of inert solvents (not less than 14-15% of the total weight of the mixture) with appropriate boiling points: xylene, cumene, pseudocumene, white spirits with boiling limits 150-160°. Stirring eliminates the possibility of local superheating while the solvent lowers the heat effect of the isomerization making it practically nonhazardous and at the same time it aids the monomolecular course of the reaction by separating the molecules of tris-β,β',β"-chloroethyl phosphite from each other. This leads to the increased yields of di-β,β'-chloroethyl ester of β-chloroethylphosphonic acid. In this manner we carried out the isomerization of tris-β,β',β"-chloroethyl phosphite taking into the reaction up to 2 kilograms of the substance per batch (instead of 270 g as described earlier [2]).

The safe isomerization of tris-β,β',β"-chloroethyl phosphite makes the dichloride of β-chloroethylphosphonic acid [2] a substance that is accessible in any desired amount, the same being true of derivatives of β-chloroethylphosphoric acid [3] and vinylphosphonic acid [4, 5], which was practically impossible previously. The preparation of the dichloride of β-chloroethylphosphonic acid according to Kinnear and Perren [6] is practicable for only small amounts of the substance. Below we give the results of some typical experiments with isomerization of tris-β,β',β"-chloroethyl phosphite (see table).

$P(OCH_2CH_2Cl)_3$ (in g)	Solvent and its amount (in g)	Time of isomerization at 150-164° (in hours)	Amt. of distilled $ClCH_2CH_2PO(OCH_2CH_2Cl)_2$ in %	Undistillable residue (in g)
504	Xylene 87	7	58	140
40	White spirits 40	17	50	17
100	Pseudocumene 100	12	60	25
910	Cumene 390	12	67	240

White spirits proved to be the least suitable of the solvents tried while cumene was the best when used in amounts of 25-30% of the total weight of the mixture.

EXPERIMENTAL

One of typical experiments. Into a pot made of stainless steel provided with a stirrer, thermometer and a reflux condenser there was placed a mixture of 910 g of tris-β,β',β"-chloroethyl phosphite and 390 g of dry cumene. The mixture was stirred energetically and refluxed for 12 hours, during which time the boiling point of the reaction mixture gradually dropped owing to formation of ethylene chloride [2] from 158° to 153°. After cooling, cumene was distilled from the mixture (at 40-60 mm and 40-100°) and the reaction product was distilled in vacuum (4 mm) until decomposition began in the sirupy residue. The fraction with the boiling range of 155-170° (620 g) was redistilled once again and gave 610 g (67%) of pure di-β,β'-chloroethyl ester of β-chloroethylphosphonic acid. This was a colorless transparent liquid which gradually crystallized on standing; b.p. 161-163° (4 mm), $n^{20}D$ 1.4844, d^{20}_4 1.3910, which values agree with the literature data [1].

Experiments with the other solvents were run analogously to the typical experiment with a small change only in the case of xylene (when a certain thermal effect was observed) the change consisting in that the mixture was rapidly heated to 130-133° and the subsequent elevation of temperature to the initial boiling of the mixture was made more slowly.

SUMMARY

A safe method of isomerization of tris-β,β',β"-chloroethyl phosphite was developed, which permits the preparation of di-β,β'-chloroethyl ester of β-chloroethylphosphonic acid in yields of 63-67%.

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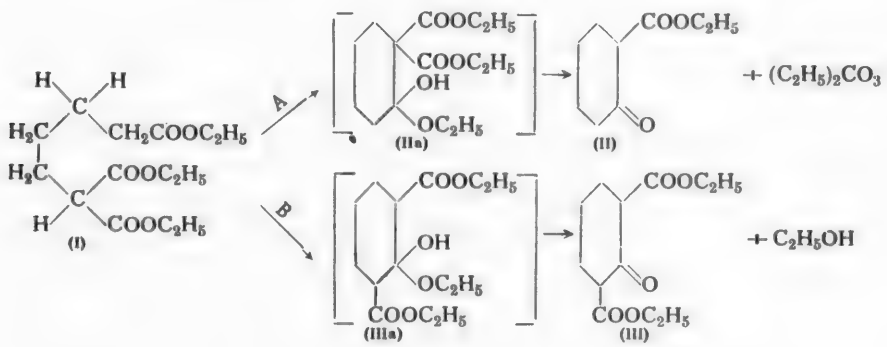
A STUDY IN THE FIELD OF THE DIECKMANN REACTION

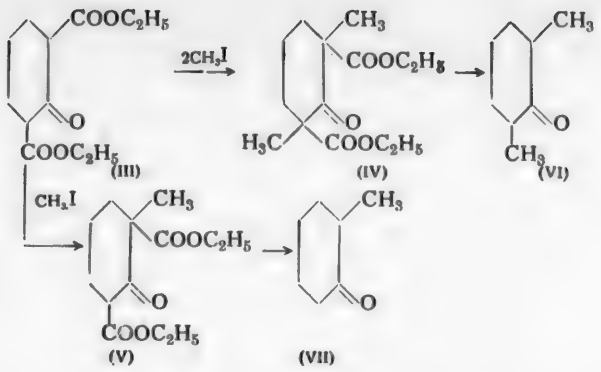
V. CYCLIZATION OF DIETHYL ESTER OF α-CARBETHOXYPIMELIC ACID

N. S. Vul'fson and V. I. Zaretskii

During the development of some work on the investigation of the orientation of cyclization of compounds by the Dieckmann reaction [1] we studied the cyclization of diethyl ester of α-carbethoxypimelic acid. It was shown earlier [2] that in cyclization of diethyl ester of α-methylpimelic acid there is formed only 2-methyl-6-carbethoxycyclohexanone. One might expect that under the influence of the electronegative α-carbethoxy group, the cyclization of the diethyl ester of α-carbethoxypimelic acid (I) would proceed in the direction opposite to that described for the diethyl ester of α-methylpimelic acid and thus lead to the formation of 2-carbethoxycyclohexanone (II) with simultaneous cleavage of diethyl carbonate.



However in running the reaction in boiling xylene in the presence of powdered sodium we obtained 2,6-dicarbethoxycyclohexanone (III) in 57% yield. It should be noted that the cyclization of ester (I) in benzene in the presence of powdered sodium or in alcoholic solution of sodium ethoxide fails to proceed to all practical purposes (the original ester(I)is recovered) while the cyclization of tetraethyl esters of pentane- and 2-methylpentane, 1,1,5,5-tetracarboxylic acid in alcoholic solution of sodium ethoxide is accompanied by cleavage of diethyl carbonate and leads to the formation of β-keto ester (III) (yield about 35% [3]) and 3-methyl-2,6-dicarbethoxycyclohexanone (yield about 44% [1]) respectively. The formation of β-keto ester (III) in the cyclization of ester (I) is evidently explicable by the presence of steric hindrance whichblocks the course of the reaction in direction A with the intermediate formation of hemiacetal (IIa), while there exists a more facile path, from the steric viewpoint, which is designated as B (above) which leads to the formation of intermediate hemiacetal (IIIa). The structure of β-keto ester (III) was proved by its methylation with methyl iodide to the corresponding 2,6-dimethyl-(IV) and 2-methyl-2,6-dicarbethoxycyclohexanone (V) with the subsequent hydrolysis and decarboxylation to the known 2,6-dimethyl-(VI) and 2-methylcyclohexanones (VII).



The initial diethyl ester of α-carbethoxypimelic acid was synthesized by us by two methods: a) starting with adipic acid, through its monoethyl ester, its silver salt and ethyl ester of δ-bromovaleric acid [4] with subsequent malonic ester synthesis, and by b) starting with 1,1,1,5-tetrachloropentane, through δ-chlorovaleric acid [5] and its ethyl ester with subsequent malonic ester synthesis according to method [6] in the presence of sodium iodide.

$$HOOC(CH_2)_4COOH \longrightarrow C_2H_5OOC(CH_2)_4COOH \longrightarrow C_2H_5OOC(CH_2)_4COOAg \longrightarrow$$
$$\longrightarrow Br(CH_2)_4COOC_2H_5$$
$$CCl_3(CH_2)_3CH_2Cl \longrightarrow Cl(CH_2)_4COOH \longrightarrow Cl(CH_2)_4COOC_2H_5 \longrightarrow \downarrow$$
$$\longrightarrow (C_2H_5OOC)_2CH(CH_2)_3CH_2COOC_2H_5$$
$$(I)$$

EXPERIMENTAL

Monoethyl ester of adipic acid was prepared by a modified method of Swann jr., Ehler and Buswell [7]. In order to obtain a product free of diethyl ether, the treatment of the reaction mixture was changed thus: the mixture after the reaction had been completed was left overnight at 15-20°, and was then filtered from unreacted adipic acid, the filtrate being poured into an equal volume of water, followed by addition of concentrated solution of sodium hydroxide to bring the mixture to a weakly acid test with Congo red and followed by extraction with benzene, taken in equal volume. The unreacted adipic acid was dissolved in 15% sodium carbonate solution and the solution was extracted with benzene, the extract being combined with the main benzene solution, while the adipic acid was recovered from the aqueous layer by acidification with hydrochloric acid; the recovered adipic acid was used again for the preparation of the monoethyl ester.

The benzene solution was repeatedly extracted with 15% sodium carbonate solution, then washed with water until neutral to Brilliant green paper, was then dried and distilled, collecting diethyl ester of adipic acid which was used in subsequent experiments. The sodium carbonate extract was combined with the main aqueous solution (after extraction with benzene), acidified with concentrated hydrochloric acid until strongly acidic to Congo red, extracted 4-5 times with ether, and the ethereal extract was dried with sodium sulfate and distilled in vacuum. The yield of monoethyl ester of adipic acid was 61.8% (taking into account the recovery of adipic acid); b.p. 129-132.5° at 2 mm; m.p. (freezing) 27.4°. According to literature data, b.p. 155-157° at 7 mm [7], m.p. 29.9°[4].

Ethyl ester of δ-bromovaleric acid. This was prepared from monoethyl ester of adipic acid according to [4]: a) silver salt, yield 70% (calculated on silver salt of monoethyl adipate), b.p. 71° at 2 mm, 69.5° at 1.5 mm, $n^{20}D$ 1.4605, d^{20}_4 1.3085. According to literature data: b.p. 101-103° at 10 mm [4], $n^{20}D$ 1.4582, d^{20}_4 1.3043 [8].

δ-Chlorovaleric acid. This was prepared by hydrolysis of 1,1,1,5-tetrachloropentane [5]. The starting material had b.p. 64.5-70.25° at 2.5 mm, $n^{20}D$ 1.4865, d^{20}_4 1.3430. According to the literature data: b.p. 112° at 24 mm, $n^{25}D$ 1.4859, d^{25}_4 1.3416 [9]. The yield of δ-chlorovaleric acid was 52.5%; b.p. 101.5° at 2.5 mm, 101.5° at 2 mm, freezing point 18.25°, $n^{20}D$ 1.4545, d^{20}_4 1.1644. According to literature data: b.p. 122-124° at 8 mm, $n^{25}D$ 1.4525, d^{25}_4 1.1667 [5]; m.p. 18° [10].

Ethyl ester of δ-chlorovaleric acid. A mixture of 95 g of δ-chlorovaleric acid, 300 ml of benzene, 70 ml of anhydrous alcohol and 13.5 ml of concentrated sulfuric acid was refluxed for six hours, cooled, poured into 500 ml of water, the mixture being then neutralized with 15% sodium carbonate solution until alkaline to Brilliant yellow paper, the benzene layer washed with water until neutral to Brilliant yellow paper, then dried with sodium sulfate and distilled, yielding 99 g (86%) of the ester with b.p. 53.5° at 1.5 mm, 52.5° at 1 mm, $n^{20}D$ 1.4305, d^{20}_4 1.0518. According to the literature data: b.p. 90° at 13 mm, d^{20} 1.054 [10].

Ethyl ester of α-carbethoxypimelic acid. a) From ethyl ester of δ-bromovaleric acid. Malonic ester (117 g) was added to the solution of sodium ethoxide (from 5.4 g of sodium and 100 ml of anhydrous alcohol) and the solution was heated to boiling (about 85°) while over thirty minutes 49.2 g of ethyl ester of δ-bromovaleric acid was being added dropwise. The mixture was refluxed three hours longer (pH of the solution was about 7.5), the alcohol was distilled from it (finally under slight vacuum), the residue was cooled, poured into 200 ml of water, extracted with benzene (200 and 100 ml portions used), the benzene solution was washed with water, dried over sodium sulfate and distilled. The yield of the ethyl ester of α-carbethoxypimelic acid was 75.5%; b.p. 146.5-150° at 2 mm, $n^{20}D$ 1.4380, d^{20}_4 1.0561. According to the literature data: b.p. 147-149° at 2 mm, $n^{20}D$ 1.4389, d^{20}_4 1.0568 [6].

b) From ethyl ester of δ-chlorovaleric acid. The product was prepared by method [6]; yield 83%, b.p. 142-143° at 1 mm.

Cyclization of diethyl ester of α-carbethoxypimelic acid. To the suspension of 4.7 g of powdered sodium in 150 ml of dry xylene there was added rapidly 43.2 g of ethyl ester of α-carbethoxypimelic acid and 0.3 ml of anhydrous alcohol. The mixture was stirred energetically until the termination of self-heating of the mass (about 10 minutes; the temperature rises to 68°), after which it was heated on an oil bath at the boiling point (134.5°) and refluxed with stirring until the boiling point of the reaction mixture ceased to decline (5-6 hours; the boiling point drops to about 112°). The mixture was cooled, poured into 150 g of ice, cooling externally with ice-salt mixture (the temperature of the reaction mass should be from −5° to −7°) and neutralized with dilute hydrochloric acid (1 : 1) to acid test with Congo red (at temperature of −1.5° to −3°). The layers were separated, the aqueous layer was extracted with 75 ml of benzene, the combined organic layer was washed with 30 ml of 5% sodium carbonate, then with water until neutral to Brilliant yellow paper, dried over sodium sulfate, freed of the solvent by distillation, and the residue was distilled, collecting the following fractions: 1st b.p. 92° at 3 mm, 136.5° at 3.5 mm, 2.4 g, $n^{20}D$ 1.4730; 2nd b.p. 136.5-138° at 3.5 mm, 2.9 g, $n^{20}D$ 1.4760; 3rd b.p. 138-140° at 3.5 mm, 15.9 g, $n^{20}D$ 1.4750, d^{20}_4 1.1203, MR_D 60.87 (calculated for the enol 59.78; calculated for the ketone 58.74); 4th b.p. 144-150° at about 5 mm, 0.6 g, $n^{20}D$ 1.4735; 5th b.p. 150° at 4.5 mm, 152° at 6-7 mm (with decomposition), 1.7 g, $n^{20}D$ 1.4740.

Analysis of the 3rd fraction:

Found %: C 59.66; H 7.56. $C_{12}H_{18}O_5$. Calculated %: C 59.50; H 7.44.

The first, fourth and fifth fractions were combined and redistilled obtaining thereby an additional 1.9 g of the keto ester (III) with b.p. 139-142° at 3.5 mm, $n^{20}D$ 1.4755 (6th fraction). All the fractions collected were colorless and gave an intensely violet color with ferric chloride. The second, third and sixth fractions thickened after some time owing to the separation of crystals of the keto form [3]. The yield of 2,6-dicarbethoxycyclohexanone (fractions 2, 3 and 6) was 57%. According to the literature data: b.p. 165-175° at 12 mm, 165-165.5° at 12 mm (enol), $n^{18.5}D$ 1.4692, $d^{18.5}_4$ 1.1239 [3].

1-Phenyl-3,4,1',2'-hexahydrobenzo-3-carbethoxy-5-pyrazolone. A mixture of 1.2 g of 2,6-dicarbethoxycyclohexanone and 0.55 g of phenylhydrazine was heated on a steam bath for one hour. It was then cooled to 15-20° and dissolved with stirring in 2 ml of ether. Approximately an hour after there began the crystallization of the pyrazolone. The mixture was left overnight, filtered and washed with ether. The yield was 1.23 g (86%); m.p. 150-150.5°; after boiling in ether, m.p. 151-151.5°. According to the literature data: m.p. 151-152° [3].

2,6-Dimethyl-2,6-dicarbethoxycyclohexanone. To the cooled solution of 17 g of 2,6-dicarbethoxycyclohexanone in 34 ml of anhydrous methanol there was added 12 ml of methyl iodide, the mixture being cooled to −15°, after which a solution of sodium methoxide (from 3.5 g of sodium and 42 ml of anhydrous methanol) was added over about 5 minutes with stirring at the temperature of from −15° to −7°. The mixture was stirred for four hours at the temperature of −2° to 0° and was left overnight at about 0°. It was then refluxed, again with stirring,

until it became neutral to Brilliant yellow test paper (2 hours), after which the methanol was distilled from the mixture on a steam bath (the volume of distillate was about 65 ml). The residue was cooled, poured into 300 ml of water, extracted four times with ether and the ethereal extract washed with 15% potassium hydroxide solution (three times with 25 ml) and with water until neutral. The solution was dried over sodium sulfate, the ether was distilled from it and the residue was distilled yielding 2,6-dimethyl-2,6-dicarbethoxycyclohexanone in 14.1 g yield (75%); b.p. 113-116° at 2 mm, $n^{20}D$ 1.4620-1.4625; the product contains traces of the unmethylated material since it gives a barely visible color test with ferric chloride, which appears after 3-5 minutes. For purification the product was dissolved in 300 ml of ether and was washed with cold 15% potassium hydroxide solution until the test with ferric chloride became negative (15 washes with 25 ml each), followed by washing with water until neutral to Brilliant yellow test paper, after which it was dried and distilled yielding 9.8 g of pure 2,6-dimethyl-2,6-dicarbethoxycyclohexanone; b.p. 123.5-126.5° at 3 mm, $n^{20}D$ 1.4615, d^{20}_4 1.086, MR_D 67.84 (the calculated value is 67.97). According to the literature data: b.p. 142° at 6 mm [11].

2,6-Dimethylcyclohexanone. A hot solution of 11 g of potassium hydroxide (8.7 g calculated as 100% substance) in 16.5 ml of anhydrous methanol was chilled rapidly to −5° and to the resulting thin suspension there was added with stirring and cooling to from −5° to +1° a solution of 8.8 g of 2,6-dimethyl-2,6-dicarbethoxycyclohexanone in 12 ml of anhydrous methanol. The mixture was stirred at 18-20° for about three hours and was left at this temperature for 12 days. The reaction mixture was then poured into 150 ml of water (at about 10°) and extracted with ether three times; the ethereal extract was washed with water until neutral to Brilliant yellow test paper. The aqueous layer combined with the wash waters from the ethereal layers was treated with 60 ml of concentrated sulfuric acid and was steam distilled. The distillate was extracted five times with ether, the ethereal solution was added to the extract from the alkaline reaction mixture (after pouring into water) and the combined ethereal solution was dried over sodium sulfate and distilled, yielding 2,6-dimethylcyclohexanone; yield 2.1 g (50.5%; b.p. 167-170.5° at 743 mm, $n^{20}D$ 1.4475-1.4480, d^{20}_4 0.9087. According to the literature data: b.p. 170-172°, $n^{20}D$ 1.4481, d^{20}_4 0.9122 [12]. Semicarbazone, m.p. 181-182° (from anhydrous alcohol). According to literature data: m.p. 183° [13].

Found %: C 59.12; H 9.52. $C_9H_{17}ON_3$. Calculated %: C 59.03; H 9.29.

2-Methyl-2,6-dicarbethoxycyclohexanone. To a cooled solution of 18.2 g of 2,6-dicarbethoxycyclohexanone in 34 ml of anhydrous methanol there was added 6.5 ml of methyl iodide, the mixture was cooled to −16° and treated with stirring at from −16° to −12.5° over seven minutes with a solution of sodium methoxide (from 1.9 g of sodium in 30 ml of anhydrous methanol) after which the mixture was left overnight at −3°. Then the mixture was refluxed for one hour, freed of methanol by distillation, the residue was cooled, poured into 300 ml of water, extracted four times with ether, the ethereal solution was washed with water and dried with anhydrous sodium sulfate. Ether was distilled from this solution and the residue was distilled in vacuum yielding 2-methyl-2,6-dicarbethoxycyclohexanone; yield 14 g (72.8%), b.p. 112-114° at 1 mm (by the literature data b.p. 142-145° at 6 mm [11]), $n^{20}D$ 1.4645-1.4655, d^{20}_4 1.0986; the substance gave an intense violet color with ferric chloride; MR_D 64.21 (for the enol of calculated value is 64.40; for the ketone it is 63.37).

2-Methylcyclohexanone. 2-Methyl-2,6-dicarbethoxycyclohexanone (14 g) was hydrolyzed and decarboxylated analogously to 2,6-dimethyl-2,6-dicarbethoxycyclohexanone and yielded 2-methylcyclohexanone in a 2.3 g yield (37.3%); b.p. 162.5-166° at 730 mm, $n^{20}D$ 1.4485, d^{20}_4 0.9224. According to the literature data: b.p. 166°, $n^{20}D$ 1.4483, d^{20}_4 0.9231 [15]. Semicarbazone, m.p. 188.5-189° (from anhydrous alcohol). According to the literature data: m.p. 189° [16]. It did not give a depression in a mixed melting point with the semicarbazone of 2-methylcyclohexanone.

SUMMARY

The cyclization of diethyl ester of α-carbethoxypimelic acid in the Dieckmann reaction was investigated. It was shown that the primary reaction product is 2,6-dicarbethoxycyclohexanone. The structure of 2,6-dicarbethoxycyclohexanone was proved by its methylation with methyl iodide to the mono- and the dimethyl derivatives and by the subsequent hydrolysis and decarboxylation of these to 2-methyl- and 2,6-dimethylcyclohexanones, respectively.

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REPLACEMENT OF HALOGEN IN AZO COMPOUNDS

I. REPLACEMENT OF CHLORINE IN 2-CHLOROPHENYLAZO-2'-NAPHTHOL BY ALKOXY GROUPS

B. I. Stepanov, M. A. Salivon, V. F. Lagidze and L. A. Dediukhina

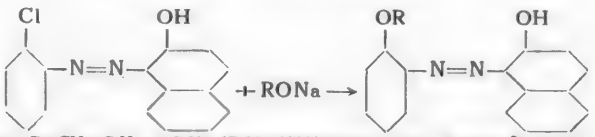
As is known [1], the replacement of an aromatically bound atom of halogen by other substituents is realized with considerably more difficulty than the analogous reactions in the aliphatic series and it is only the activating influence on the part of electrophilic substituents as well as the catalytic action of copper and its compounds that make it possible for one to conduct the substitution reactions at temperatures under 200°.

The data on the effect of the azo group on the mobility of an aromatically bound halogen are scanty. According to Borsche and Exss [2], an azo group in the molecules of isomeric mononitrochlorobenzenes facilitates the replacement of chlorine in the reaction with amines and alcoholates, but it does so to a lesser degree than do the nitro, nitrile and the carboxyl groups. According to Badger, Cook and Vidal [3], the introduction of an azo group into the molecule of chlorobenzene increases the yield of the substitution product of chlorine in the reaction with piperidine by approximately 1.5-fold while the nitro group under these conditions increases the yield by almost 10-fold. According to the patent data of Sieglitz and co-workers [4, 5], the replacement of chlorine and bromine in the molecules of azo dyes, which do not contain any electrophilic substituents in ortho- and para-positions in respect to these atoms, by alkoxy groups and residues of alkyl- and arylsulfinic acids requires the temperature of the order of 130-170° and, in a number of cases, the presence of copper powder. At the same temperature the replacement of chlorine by the hydroxy group proceeds in the molecule of an azo dye containing a carboxy group in ortho-position in respect to the atom of chlorine [6] and only the presence of nitro and sulfo groups in ortho- and para-positions with respect to the chlorine atom permits one to realize such a substitution at the boiling point of an alkaline aqueous solution of the azo dye [7].

For these reasons there is much interest in the patents by D. Delfs and co-workers [8-10] according to which the chlorine atom in molecules of o-chloro-o'-hydroxy- azo dyes is replaced in the presence of copper salts by hydroxy, alkoxy, alkylamino and some other groups by even brief heating with aqueous alkalies, alcoholates etc. at temperatures of the order of 70-100°. The amount of copper salt used in the process exceeds by a large margin that used for catalytic reactions, while, according to the patent data, the end product is obtained in the form of a copper complex. Only the chlorine atom in ortho-position in respect to the azo group suffers the replacement (as, for example, it is in examples of Sieglitz patents [4, 5]). The significance of copper is underlined by the circumstance that the replacement of chlorine by a hydroxy group in the same dyes in aqueous alkaline solution but in the presence of chromium oxide [11] (with formation of chromium-bearing complexes) requires the temperature of the order of 130-140°. The data of the patent by Schmelzer and Bayer [12] are in the state of known contradiction with those of Delfs' patent, as the former indicate that the formation of copper complexes of o,o'-dihydroxy azo dyes, in the reaction of o-chloro-o'-hydroxy azo dyes with alkalies and copper salts, proceeds only at temperatures of 140-150°.

Considering the theoretical significance of the problem of the reasons for the anomalous mobility of the halogen atoms located in the ortho-position in respect to the azo group, as well as the preparative possibilities opened by this reaction, since the resulting azo dyes are subject to facile reduction cleavage, we considered it interesting to study the reaction in more detail, especially since the data on the replacement of the halogen in azo compounds are contained almost totally in the patent literature.

We used 2-chlorophenylazo-2'-naphthol, i.e., the azo dye from 2-chloroaniline and 2-naphthol, for the starting o-halo-o'-hydroxy azo compound. In its reaction with sodium methoxide, prepared either by the action of metallic sodium or sodium hydroxide on methyl alcohol, and copper sulfate in methyl alcohol there was prepared in quantitative yield the 2-methoxyphenylazo-2'-naphthol in the form of the complex compound with copper, after heating under a reflux condenser on a water bath. The free methoxy substituted dye was readily liberated by the decomposition of the complex by heating with hydrochloric acid. In a control experiment, in the absence of copper sulfate, there was isolated only the starting chlorine-containing dye. Analogous results were obtained in the reaction of the original dye with sodium ethoxide in ethyl alcohol. Here, also in the presence of copper sulfate, the chlorine atom was quantitatively replaced by the ethoxy group at the boiling point of the reaction mixture (heating on a water bath). The reaction of the chlorine-containing dye with alcoholates of higher boiling alcohols – n-butyl, isoamyl, n-hexyl and n-octyl – was run in an excess of the appropriate alcohol at 100-110°, while the reaction with the alcoholate of octadecyl alcohol was run in toluene medium at 115-118°. Products of replacement of chlorine by the alkoxy groups were obtained in high yields in all cases, while the control experiments, in the absence of the copper salt, gave negative results.



where: R=CH_3, C_2H_5, n-C_4H_9, $(CH_3)_2CHCH_2CH_2$, n-C_8H_{13}, n-C_8H_{17} & n-$C_{18}H_{37}$

In this manner the reaction is realized in the presence of a copper salt quite readily, which fact speaks for the high order of mobility of the chlorine atom in the given dye under the above conditions.

Some of the dyes prepared by us turned out to be suitable for dyeing acetate and polyamide fibers by the suspension technique.

The corresponding ethers of o-aminophenol (2-alkoxyanilines), which were characterized in the form of hydrochloride salts of benzoyl derivatives, except for the ether with the octadecyl residue which was quite stable in the form of the free base, owing to the facile oxidizability of the majority of these ethers, were prepared by the reductive cleavage of the alkoxy substituted dyes. It is interesting to note that the free base of this amine (2-octadecoxyaniline) is formed already in the process of recrystallization of its hydrochloride salt from methy alcohol. Among the ethers of o-aminophenol prepared by us, the ethers with butyl [13, 14], isoamyl [15], n-hexyl [14] and n-octyl [14] residues, have been described previously in the form of free bases.

EXPERIMENTAL*

The starting dye was prepared by diazotization of 2-chloroaniline and coupling with 2-naphthol; m.p. 167° (from glacial acetic acid [16]).

Replacement of chlorine by methoxy group. Four g of the starting dye, ground with 2 g of copper sulfate, was introduced into the solution of sodium methoxide prepared by the reaction of 1 g of metallic sodium (or 2.5 g of sodium hydroxide) with 40 ml of methyl alcohol. The mixture was refluxed for four hours with stirring on a water bath, after which the alcohol was distilled off and the residue was boiled for 15-20 minutes with 50 ml of concentrated hydrochloric acid. After dilution with water, the precipitate was filtered off, washed until the filtrate became free of chloride ions and dried at 70°. Its weight was 3.9 g (100%). After recrystallization from glacial acetic acid the dye was obtained in the form of orange-red bronze-appearing powder with m.p. 178°. The test for chlorine was negative. A mixed melting point with the azo dye from o-anisidine and 2-naphthol (m.p. 178°; the literature indicates m.p. 180° – from glacial acetic acid [16], or 178° – from alcohol [17]) showed no depression.

Replacement of chlorine by ethoxy group. The amounts of the starting materials, selected appropriately, and the conditions for running the reaction and working-up the product were the same as in the above experiment; the duration of heating on the water bath was six hours. There was obtained 3.9 g (94.4%) of copper-free dye.

*With participation by V. S. Zenkevich.

After recrystallization from glacial acetic acid the dye was obtained in the form of a red shiny powder with m.p. 145°. The test for chlorine was negative. A mixed melting point with the azo dye from o-phenetidine and 2-naphthol, which melted at 145° (the literature indicates m.p. 145° – from glacial acetic acid [16] and 138° – from alcohol [17]) showed no depression.

Replacement of chlorine by n-butoxy group. Eight g of the starting dye, ground with 4 g of copper sulfate, was introduced into the solution of sodium butoxide prepared by the action of 2 g of metallic sodium on 80 ml of n-butyl alcohol (b.p. 117°) and the mixture was heated with stirring for eight hours at 100°. After that the reaction mixture was diluted with 200 ml of water and brought to boiling. After cooling, the precipitate was filtered off and boiled for 20 minutes with 100 ml of concentrated hydrochloric acid. The precipitate was filtered off after dilution with water, washed until the filtrate became free of the chloride ions and dried at 70°. Its weight was 8.5 g (93.8%). After recrystallization from glacial acetic acid the dye was obtained in the form of red needle shaped crystals, m.p. 116-117°. The test for chlorine was negative. The dye was soluble in benzene, toluene, glacial acetic acid, methyl and ethyl alcohols and insoluble in water.

Found %: C 75.48, 75.28; H 6.51, 6.41; N 9.04; 8.86. $C_{20}H_{20}O_2N_2$. Calculated %: C 75.00; H 6.25; N 8.75.

Preparation of 2-butoxyaniline. To a solution of stannous chloride, prepared by the reaction of 8 g of metallic tin with 75 ml of concentrated hydrochloric acid with heating, there was added 70 ml of water and 5 g of the butoxy substituted dye. The mixture was refluxed until it became colorless, after which it was left overnight. The resulting precipitate was filtered off and treated with 25 ml of 5% solution of sodium hydroxide to which had been added about 0.3 g of sodium hydrosulfite for protection of the amine from oxidation. 2-Butoxyaniline was extracted with ether and, after separation of the ethereal layer, was precipitated by a stream of hydrogen chloride passed into the solution. The precipitate was filtered off and recrystallized from ethyl alcohol. There was obtained 1.9 g of the hydrochloride salt in the form of long thin plates, m.p. 146-148°.

Found %: N 7.15, 7.09. $C_{10}H_{16}ONCl$. Calculated %: N 6.94.

For preparation of the N-benzoyl derivative, 0.15 g of the hydrochloride salt of 2-butoxyaniline was shaken for ten minutes with 2 ml of 20% solution of sodium hydroxide and 0.5 ml of benzoyl chloride, after which the mixture was diluted with water and the precipitate was filtered off, washed and dried. Its weight was 0.15 g. After recrystallization from dilute methyl alcohol, the benzoyl derivative was obtained in the form of greatly attenuated flat hexagons; m.p. 45-46°.

Found %: C 75.68, 75.80; H 7.36, 7.22; N 5.39, 5.31. $C_{17}H_{19}O_2N$. Calculated %: C 75.83; H 7.06; N 5.20.

Replacement of chlorine by 3-methylbutoxy group. The amounts of the starting materials (isoamyl alcohol with b.p. 132°) and the conditions of running the reaction were as in the previous experiment. The reaction mixture was diluted with water, the precipitate was filtered off, boiled twice with water, then for fifteen minutes with 100 ml of concentrated hydrochloric acid. After dilution with water the reaction product was precipitated in the form of a tarry viscous mass which hardened on cooling. The precipitate was ground up and again treated with concentrated hydrochloric acid (50 ml) for fifteen minutes at reflux with stirring. The again triturated precipitate was washed with water until the filtrate became clear of chloride ions and was dried in air. Its weight was 6.5 g (68.8%). After recrystallization from glacial acetic acid and acetone the dye was obtained in the form of bundles of thin needles; m.p. 128°. The test for chlorine was negative. The dye is soluble in benzene, toluene, methyl and ethyl alcohols, glacial acetic acid; it is insoluble in water.

Found %: C 75.2, 75.31; H 7.07, 6.96; N 8.64, 8.51. $C_{21}H_{22}O_2N_2$. Calculated %: C 75.45; H 6.58; N 8.38.

Preparation of 2(3'-methylbutoxy)aniline. To a solution of stannous chloride (from 2 g of metallic tin and 20 ml of concentrated hydrochloric acid) there was added 20 ml of water and 1 g of the methylbutoxy substituted dye and the mixture was refluxed until it became colorless. The reaction mixture was made alkaline with 30 ml of 40% solution of sodium hydroxide (with addition of 0.3 g of sodium hydrosulfite) and methylbutoxyaniline was steam distilled and extracted from the distillate with ether. The ethereal layer was separated and treated with 5 ml of concentrated hydrochloric acid. After evaporation of ether and concentration of the residue on a steam bath there was obtained 0.45 g of the hydrochloride salt of (2(3'-methylbutoxy)-aniline in the form of thin colorless needles (after recrystallization from water acidified by a few drops of hydrochloric acid); m.p. 165-165.5°.

Found %: N 6.69. $C_{11}H_{18}ONCl$. Calculated %: N 6.49.

For preparation of the n-benzoyl derivative 0.1 g of the hydrochloride of 2(3'-methylbutoxy)aniline was benzoylated as in the case of 2-butoxyaniline. There was obtained 0.16 g of the benzoyl derivative; flat colorless needles, after recrystallization from methyl alcohol; m.p. 58-59°.

Found %: C 76.51, 76.37; H 7.51, 7.65; N 4.96; 5.08. $C_{18}H_{21}O_2N$. Calculated %: C 76.32; H 7.42; N 4.95.

Replacement of chlorine by hexoxy group. The amounts of the starting dye, copper sulfate and metallic sodium and the conditions for running the reaction were the same as in experiments with butyl and isoamyl alcohols; n-hexyl alcohol, b.p. 157°, was taken in the volume of 40 ml. After cooling of the reaction mixture the precipitate was filtered off, the hexyl alcohol was distilled in vacuum from the filtrate and the residue was combined with the main precipitate. The product was boiled twice with water, then with concentrated hydrochloric acid (100 ml), after which the mixture was diluted with water, the dye was filtered off, washed until the filtrate became free of chloride ions, and dried in air. Its weight was 8.75 g (88.8%). After recrystallization from glacial acetic acid and acetone the dye was obtained in the form of flat elongated rectangles; m.p. 90-90.5°. The test for chlorine was negative. The dye is soluble in toluene, methyl and ethyl alcohols, acetone and glacial acetic acid; it is insoluble in water.

Found %: C 75.51, 75.41; H 6.62, 6.79; N 8.12, 8.08. $C_{22}H_{24}O_2N_2$. Calculated %: C 75.86; H 6.90; N 8.05.

Preparation of 2-hexoxyaniline. The reductive cleavage of the hexoxy substituted dye and the isolation of the hydrochloride salt of 2-hexoxyaniline were run as in the preparation of 2(3'-methylbutoxy)aniline. After recrystallization from dilute methyl alcohol the hydrochloride salt of 2-hexoxyaniline was obtained in the form of colorless needles, m.p. 159-159.5°.

Found %: N 6.25. $C_{12}H_{20}ONCl$. Calculated %: N 6.10.

For preparation of the N-benzoyl derivative 0.1 g of the hydrochloride salt of 2-hexoxyaniline was benzoylated as in the case of 2-butoxyaniline. There was obtained 0.13 g of the benzoyl derivative; flat colorless needles, after recrystallization from methyl alcohol; m.p. 48-48.5°.

Found %: C 76.97, 76.85; H 7.95, 7.87; N 4.89, 4.81. $C_{19}H_{23}O_2N$. Calculated %: C 76.76; H 7.74; N 4.71.

Replacement of chlorine by octoxy group. The amounts of the starting materials were the same as in the experiment with hexyl alcohol, except for the use of n-octyl alcohol (b.p. 194-195°) and heating for ten hours at 110-115°. After termination of heating, the reaction mixture was diluted with water with energetic stirring, and the precipitate was filtered off. The filtrate rapidly separated into layers and the alcohol layer was separated and freed of octyl alcohol in vacuum at 105-110°. The residue was combined with the main precipitate. The combined product was boiled for 30 minutes with 100 ml of concentrated hydrochloric acid, after which the mixture was cooled, diluted with water, the dye was filtered off and freed of chloride ions by washing and repeated boiling with water. Its weight was 9.5 g (89.2%). After recrystallization from ethyl alcohol the dye was obtained in the form of bundles of thin needles; m.p. 98.5°. The test for chlorine was negative. The dye is readily soluble in the cold in carbon tetrachloride, chloroform, benzene and toluene; in hot acetone, ethyl and methyl alcohols; it is insoluble in water.

Found %: C 76.41, 76.50; H 7.76, 7.65; N 7.63. $C_{24}H_{28}O_2N_2$. Calculated %: C 76.59; H 7.45; N 7.45.

Preparation of 2-octoxyaniline. The reductive cleavage of the octoxy substituted dye was run as in the preparation of 2(3'-methylbutoxy)aniline. The reaction mixture, along with the dark oily liquid which separated from it and solidified on cooling, was diluted with 70 ml of water and treated with 30 ml of 40% solution of sodium hydroxide (with addition of 0.3 g of sodium hydrosulfite), after which the 2-octoxyaniline was extracted with ether. After addition of 5 ml of concentrated hydrochloric acid and 20 ml of water to the ethereal layer there precipitated a slightly pinkish precipitate of the hydrochloride salt, which was filtered off and dried in air. After recrystallization from methyl alcohol the hydrochloride salt of 2-octoxyaniline was obtained in the form of colorless needles; m.p. 142-142.5°.

Found %: C 65.27, 65.38; H 9.24, 9.16; N 5.54, 5.63. $C_{14}H_{24}ONCl$. Calculated %: C 65.63; H 9.32; N 5.43.

For preparation of the N-benzoyl derivative 0.1 g of the hydrochloride salt of 2-octoxyaniline was benzoylated as in the case of 2-butoxyaniline. There was obtained 0.14 g of the benzoyl derivative which formed colorless platelets after recrystallization from dilute methyl alcohol; m.p. 43.5-44°.

Found %: C 77.37, 77.43; H 8.52, 8.46; N 4.47, 4.59. $C_{21}H_{27}O_2N$. Calculated %: C 77.53; H 8.30; N 4.30.

Replacement of chlorine by octadecoxy group. Four g of the initial dye was triturated with 2 g of copper sulfate and thoroughly mixed with 40 ml of toluene. The resulting suspension was introduced into a solution of sodium octadecoxide (prepared by the reaction of 20 g of n-octadecyl alcohol (m.p. 58.5°) with 1.5 g of metallic sodium at 150-160°) preheated to 95°. The mixture was heated for eleven hours at 95-100° and nine more hours at 115-118°, during which a foaming of the reaction mixture was observed. After that the toluene was distilled in vacuum, the residue was diluted with water and the precipitate was filtered off. For removal of the excess octadecyl alcohol the precipitate was treated several times with boiling methyl alcohol (total volume 300 ml), after which it was boiled for 30 minutes with 100 ml of hydrochloric acid. After dilution with water the precipitate was filtered off, washed with hot water until free of chloride ions, boiled several times with methyl alcohol (total volume 250 ml) and dried. Its weight was 5.2 g (71.2%). After recrystallization from glacial acetic acid the dye was obtained in the form of bundles of thin needles; m.p. 78.5-79.5°. The test for chlorine was negative. The dye is soluble in cold benzene, toluene, carbon tetrachloride and chloroform; in hot acetone and acetic acid; it is insoluble in water, methyl and ethyl alcohols.

Found %: C 79.18, 79.29; H 9.48, 9.36; N 5.45. $C_{34}H_{48}O_2N_2$. Calculated %: C 79.07; H 9.30; N 5.42.

Preparation of 2-octadecoxyaniline. The reductive cleavage of the octadecoxy substituted dye was run as described for the 2(3'-methylbutoxy)aniline. The precipitate formed as the result of solidification of the dark oily liquid collected on the bottom of the flask after reduction was separated, washed with water and treated with 25 ml of 5% solution of sodium hydroxide (with addition of 0.3 g of sodium hydrosulfite). Then 2-octadecoxyaniline was extracted with ether and the ethereal solution was treated with 5 ml of concentrated hydrochloric acid. After evaporation of ether, the precipitate of the hydrochloride salt of 2-octadecoxyaniline was filtered off, washed with water and dried in air. M.p. 124-125.5°.

Found %: N 3.54. $C_{24}H_{44}ONCl$. Calculated %: N 3.52.

After recrystallization of the hydrochloride salt from methyl alcohol there was isolated a quantitative yield of the free 2-octadecoxyaniline in the form of flat plates; m.p. 54.5-55.5°.

Found %: C 79.59, 79.66; H 12.09; 12.01; N 3.67, 3.65. $C_{24}H_{43}ON$. Calculated %: C 79.77; H 11.91; N 3.87.

For preparation of the N-benzoyl derivative 0.1 g of the hydrochloride salt of 2-octadecoxyaniline was benzoylated as in the case of 2-butoxyaniline. There was obtained 0.12 g of the benzoyl derivative; flat needles after recrystallization from methyl alcohol; m.p. 66.7-68°.

Found %: C 79.81; 79.93; H 10.23, 10.28; N 2.92. $C_{31}H_{47}O_2N$. Calculated %: C 80.00; H 10.10; N 3.01.

We express our gratitude to N. N. Vorozhtsov for a number of valuable suggestions.

SUMMARY

1. The replacement of chlorine atoms by alkoxy groups with methyl, ethyl, n-butyl, isoamyl, n-hexyl, n-octyl and n-octadecyl residues was realized by the reaction of sodium alcoholates with the azo dye from 2-chloroaniline and 2-naphthol.

2. It was shown that the reaction of chlorine replacement in the given o-halo-o'-hydroxy azo dye proceeds under mild conditions in the presence of a copper salt.

3. 2-Alkoxyanilines with n-butyl, isoamyl, n-hexyl, n-octyl and n-octadecyl residues were prepared by reductive cleavage of the alkoxy substituted dyes.

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REPLACEMENT OF HALOGEN IN AZO COMPOUNDS

II. REACTION OF 2-CHLOROPHENYLAZO-2'-NAPHTHOL WITH PHENOLATES

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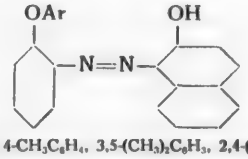
In the previous paper [1] we reported the replacement of a chlorine atom in o-chloro-o'-hydroxy azo dye by alkoxy groups. It was interesting to check the possibility of replacement of chlorine in this azo compound by aryloxy groups. The principal difference here consists of the fact that in this case the chlorine-containing dye is subjected to the action of an aqueous alkaline solution of a phenolate, i.e., conditions under which, according to Delfs [2, 3] there takes place a replacement of the chlorine atom by a hydroxy group with formation of a copper complex of the dihydroxy azo dye, rather than a reaction with an alcoholate in a practically anhydrous medium. It is interesting to note that in the examples in Delfs' patent relating to the replacement of chlorine in o-chloro-o'-hydroxy azo dyes by substituents other than the hydroxy group, the reaction with phenolates with formation of aryloxy derivatives is not described [4].

On heating under reflux at 100-110° 2-chlorophenylazo-2'-naphthol (the azo dye from 2-chloroaniline and 2-naphthol) with copper sulfate and an aqueous alkaline solution of phenol, o-, m- and p-cresols, 1,3,5- and 1,2,4-xylenols and with 4(1',1',3',3'-tetramethylbutyl)phenolate (p-iso-octylphenolate) in xylene medium there were obtained in high yields the products of replacement of the chlorine atom by the respective aryloxy groups, the yields in the majority of cases being quantitative. Thus there were prepared azo dyes which were derivatives of o-aminodiphenyl ether and its homologs.



where: Ar = C_6H_5, 2-$CH_3C_6H_4$, 3-$CH_3C_6H_4$, 4-$CH_3C_6H_4$, 3,5-$(CH_3)_2C_6H_3$, 2,4-$(CH_3)_2C_6H_3$ & 4-$(CH_3)_3CCH_2C(CH_3)_2C_6H_4$.

Control experiments in the absence of the copper salt gave negative results. In not a single case were there detected in the reaction mixture any noticeable amounts of the o,o'-dihydroxy azo dyes, i.e., the replacement of the chlorine atom by a hydroxyl group was not noted under the conditions used for the reaction (heating in aqueous alkaline medium in the presence of the copper salt).

The corresponding o-aryloxyanilines (homologs of o-aminodiphenyl ether) were prepared by reductive cleavage of some of these dyes. The dyes prepared by us were capable of dyeing acetate and polyamide fibers.

EXPERIMENTAL*

Replacement of chlorine by phenoxy, 2-, 3- and 4-methylphenoxy and 3,5- and 2,4-dimethylphenoxy groups. Eight g of the azo dye from 2-chloroaniline and 2-naphthol (m.p. 167°; see [1]) triturated with 4 g of copper sulfate and 5 ml of water was introduced into the solution of the phenolate prepared by the reaction of 40 g of the appropriate phenol with 80 ml of 30% solution of sodium hydroxide. The mixture was heated under reflux with stirring for 8-12 hours at 100-110°, after which it was diluted with 2 volumes of water and the precipitate was

* With participation by V. S. Zenkevich.

filtered off. The precipitate was heated to boiling with 5% solution of sodium hydroxide, for the removal of excess phenol, was filtered again and washed with water; in case of necessity the washing with alkali was repeated. Then the precipitate was boiled with 100 ml of concentrated hydrochloric acid, was filtered off after dilution with water, washed free of chloride ions and dried in air. The test for chlorine was negative.

There was obtained 7.1 g (73.8%) of the phenoxy substituted dye. After recrystallization from glacial acetic acid it formed thin needles with m.p. 149°. According to the literature data [6]: m.p. 135°. The dye was soluble in toluene, ethyl alcohol and glacial acetic acid and insoluble in water.

Found %: C 77.57, 77.49; H 4.80, 4.89; N 8.39, 8.48. $C_{22}H_{16}O_2N_2$. Calculated %: C 77.65; H 4.70; N 8.23.

There was obtained 9.2 g (92%) of the 2-methylphenoxy substituted dye. After recrystallization from ethyl alcohol it formed narrow flat needles with m.p. 147.5-148.5°. The dye was readily soluble in benzene, toluene and chloroform, less readily in ethyl alcohol and very poorly soluble in glacial acetic acid (even on heating); it was insoluble in water.

Found %: C 78.0, 78.1; H 5.58, 5.65; N 7.88. $C_{26}H_{16}O_2N_2$. Calculated %: C 77.97; H 5.09; N 7.91.

There was obtained 9.7 g (96.8%) of the 3-methylphenoxy substituted dye. After recrystallization from ethyl alcohol it formed small flat needles with m.p. 115-116°. The dye was soluble in benzene, toluene, chloroform, carbon tetrachloride, glacial acetic acid and ethyl alcohol and insoluble in water. A solution in concentrated sulfuric acid had a red-violet color which changed to yellow after dilution of the solution with water.

Found %: C 77.87, 77.67; H 5.17, 5.00; N 8.05, 8.37. $C_{23}H_{18}O_2N_2$. Calculated %: C 77.97; H 5.09; N 7.91.

There was obtained 9.9 g (98.8%) of the 4-methylphenoxy substituted dye. After recrystallization from glacial acetic acid it formed wide flat needles with m.p. 165.5-166.5°.

The dye was soluble in benzene, toluene, chloroform, glacial acetic acid and ethyl alcohol and was insoluble in water.

Found %: C 77.73; 77.76; H 5.20, 5.13; N 8.01. $C_{23}H_{18}O_2N_2$. Calculated %: C 77.97; H 5.09; N 7.91.

There was obtained 9.4 g (90.2%) of the 3,5-dimethylphenoxy substituted dye. After recrystallization from ethyl alcohol it formed narrow sharp needles with m.p. 138.5-139°. The dye was soluble in chloroform, benzene, toluene, glacial acetic acid and ethyl alcohol and was insoluble in water. Its solution in concentrated sulfuric acid has a cherry red color which changed to yellow on dilution of the solution with water.

Found %: C 78.17, 78.04; H 5.55, 5.65; N 7.88. $C_{24}H_{20}O_2N_2$. Calculated %: C 78.26; H 5.43; N 7.61.

There was obtained 7.6 g (70.3%) of the 2,4-dimethylphenoxy substituted dye. After recrystallization from glacial acetic acid it formed long flat needles with m.p. 158.2-159°. The dye was soluble in benzene, toluene, acetone, chloroform, glacial acetic acid and ethyl alcohol and insoluble in water.

Found %: C 78.16, 78.0; H 5.53, 5.70; N 7.91, 8.00. $C_{24}H_{20}O_2N_2$. Calculated %: C 78.26; H 5.43; N 7.61.

Replacement of chlorine by 4(1',1',3',3'-tetramethylbutyl)phenoxy group (4-iso-octylphenoxy group). 3 g of the initial dye, triturated with 1.5 g of copper sulfate was introduced into the mixture of the iso-octylphenolate and xylene prepared by the reaction of 4.4 g of iso-octylphenol with 0.5 g of metallic sodium in 40 ml of xylene with heating. The resulting mixture was heated under reflux with stirring for 15 hours at 105-110°, after which the xylene was distilled in vacuum at 80°. The residue was boiled for 30 minutes with 50 ml of concentrated hydrochloric acid, washed with water, then with 5% solution of sodium hydroxide and again with water, after which it was dried in air. The weight was 4.75 g (98.9%). The test for chlorine was negative. After recrystallization from glacial acetic acid the dye was obtained in the form of bundles of long plates with uneven edges; m.p. 142.5-143°. The dye was readily soluble in the cold in benzene, toluene, xylene, chlorobenzene, chloroform and carbon tetrachloride; it was soluble with heating in ethyl alcohol, acetone and glacial acetic acid; it was insoluble in water.

Found %: C 79.60, 79.51; H 7.17, 7.23; N 6.29, 6.39. $C_{30}H_{32}O_2N_2$. Calculated %: C 79.64; H 7.08; N 6.19.

Preparation of 2(4'-methylphenoxy)aniline (2-amino-4'-methyldiphenyl ether). To the solution of stannous chloride prepared by the reaction of 2 g of metallic tin with 35 ml of concentrated hydrochloric acid with heating, there was added 35 ml of water and 1 g of 4-methylphenoxy substituted dye and the mixture was refluxed until it

became colorless. The precipitate which formed on cooling was filtered off and was treated with 25 ml of 5% solution of sodium hydroxide with addition of 0.3 g of sodium hydrosulfite, after which the 2-(4'-methylphenoxy)aniline was extracted with ether. The ethereal layer was separated and treated with 2 ml of concentrated hydrochloric acid. After evaporation of ether from the residual aqueous layer there precipitated the hydrochloride salt of 2-(4'-methylphenoxy)aniline. Its weight was 0.47 g. After recrystallization from dilute methyl alcohol acidified by several drops of hydrochloric acid it formed flat needles with m.p. 187.5-189° (in sealed capillary). According to the literature data [15]: m.p. 220°.

Found %: C 66.60, 66.53; H 6.18, 6.09; N 6.05, 5.86. $C_{13}H_{14}ONCl$. Calculated %: C 66.24; H 5.94; N 5.94.

For preparation of the N-benzoyl derivative 0.1 g of the hydrochloride salt of 2-(4'-methylphenoxy)aniline was shaken with 2.5 ml of 20% solution of sodium hydroxide and 0.5 ml of benzoyl chloride after which the mixture was diluted with water and the precipitate was filtered off, washed and dried. Its weight was 0.11 g. After recrystallization from dilute methyl alcohol the benzoyl derivative was obtained in the form of bundles of colorless needles with m.p. 67-68°.

Found %: C 79.14, 78.96; H 5.80, 5.95; N 4.74. $C_{20}H_{17}O_2N$. Calculated %: C 79.20; H 5.61; N 4.62.

Preparation of 2-(3',5'-dimethylphenoxy)aniline (2-amino-3',5'-dimethyldiphenyl ether). The reductive cleavage of 3,5-dimethylphenoxy substituted dye was run as in the above case but the complete decolorization took place only after the reaction mixture had stood overnight and the precipitate of the hydrochloride salt of 2-(3',5'-dimethylphenoxy)aniline formed some 15 minutes after the addition of concentrated hydrochloric acid to the ethereal extract. The precipitate was filtered off, washed with a small volume of water, dried and recrystallized from methyl alcohol, after which it was obtained in the form of large colorless needles, with m.p. 186-188°.

Found %: C 67.11, 67.25; H 6.59, 6.49; N 5.72. $C_{14}H_{16}ONCl$. Calculated %: C 67.33; H 6.41; N 5.61.

For preparation of the N-benzoyl derivative 0.1 g of the hydrochloride of 2-(3',5'-dimethylphenoxy)aniline was benzoylated as described above. There was obtained 0.15 g of the benzoyl derivative which after recrystallization from methyl alcohol formed thin colorless needles with m.p. 139.5-140°.

Found %: C 79.44, 79.34; H 6.20, 6.08; N 4.22. $C_{21}H_{19}O_2N$. Calculated %: C 79.49; H 5.99; N 4.41.

Preparation of 2-(2'-4'-dimethylphenoxy)aniline (2-amino-2',4'-dimethylphenyl ether). The reductive cleavage was run as in previous cases. The hydrochloride salt of 2-(2'-4'-dimethylphenoxy)aniline was obtained, after recrystallization from dilute methyl alcohol, in the form of thin plates with m.p. 167-169°.

Found %: C 66.81, 66.89; H 6.88, 6.98; N 5.79, 5.71. $C_{14}H_{16}ONCl$. Calculated %: C 67.33; H 6.41; N 5.61.

We express our gratitude for valuable suggestions to N. N. Vorozhtsov.

SUMMARY

1. The replacement of the chlorine atom by aryloxy groups with phenyl, 2-methylphenyl-, 3-methylphenyl, 4-methylphenyl, 3,5-dimethylphenyl, 2,4-dimethylphenyl and 4-(1',1',3',3'-tetramethylbutyl)phenyl (p-isooctylphenyl) residues was realized by the reaction of sodium phenolates with the azo dye from 2-chloroaniline and 2-naphthol.

2. It was shown that the replacement of chlorine in the given o-halo-o'-hydroxy azo dye by the aryloxy groups proceeds readily in aqueous alkaline medium in the presence of a copper salt and is not accompanied by any formation of noticeable amounts of the product of replacement of chlorine by the hydroxyl group.

3. Homologs of 2-aminodiphenyl ether (2-phenoxyaniline) with methyl groups in positions 4'-, 3',5'- and 2',4'- were prepared by reductive cleavage of the aryloxy substituted azo dyes.

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*Original Russian pagination. See C. B. Translation.

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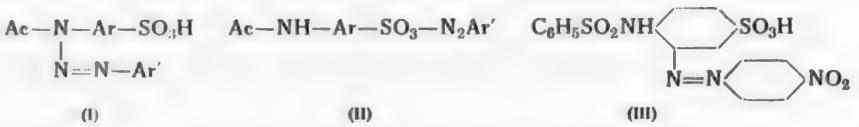
REACTION OF DIAZO COMPOUNDS WITH SULFAMIC ACID AND ITS DERIVATIVES

X. CONCERNING COLORED SALTS OF ACYLAMINOARYLSULFONIC ACIDS WITH DIAZONIUM BASES

D. Z. Zavel'skii and L. A. Lishnevskaia

In the previous papers [1, 2] we described the synthesis and the properties of arylsulfamates of diazonium compounds and discussed the reasons for their color. At that time a supposition was made that the cause for the color of these salts is the salt bond of a special character which carries the conjugation between the electron-acceptor system of the diazonium cation and the electron-donor system of the arylsulfamate anion.

There is an indication in the literature [3] that Schroeter had prepared the reaction products of diazonium salts with acylaminoarylsulfonic acids which turned out to be highly colored and quite stable. For example, acetylnaphthionic acid gave with 2-, 3- and 4-nitrophenyldiazonium compounds the correspondingly dark-red, light yellow-red and green-red crystals, while benzenesulfonylsulfanilic acid gave with the same diazonium compounds the orange-yellow, yellow and egg-yellow products. These substances turned out to be so stable that they readily underwent recrystallization from hot water. They evolved diazo nitrogen quantitatively on being boiled with water while on being heated in the dry state they ignited or charred. The author supposed at first, on the basis of the exceptional stability of these compounds, that they are diazoamino compounds [3] of type (I), but then characterized them as diazonium salts [4] of type (II) but failed to provide any information about their activity in diazo coupling reactions. For the products of reaction of 4-nitrophenyldiazonium compound with N-benzenesulfonyl substituted sulfanilic and naphthionic acids, Schroeter proposed the structure of acid azo dyes of type (III), since on being boiled with water they failed to evolve nitrogen and dyed wool from an acid bath.



(I) (II) (III)

Three years later a patent was taken out [5] on the preparation of analogous products of reaction of diazonium chlorides with arylsulfamidoarylsulfonic acids which were named as diazoamino compounds in the patent. In later patents [6, 7] the same compounds were described as stable diazonium salts. Saunders [8] in discussing these contradictions in his well-known book gave Schroeter's compounds the structure of diazo salts.

The properties of Schroeter's compounds seemed to us, by description, to be so similar to diazonium arylsulfamates which had been studied by us, that we repeated Schroeter's work with the example of benzenesulfonylsulfanilic acid which is closest in its structure to arylsulfamic acids,

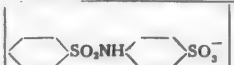
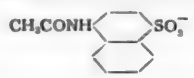
for the purpose of detailing the structure of these compounds and for a comparison of their properties, especially the color, with those of the diazonium arylsulfamates.

We synthesized benzenesulfonylsulfanilic acid, at first, by Schroeter's method [4], by dropwise introduction of benzenesulfonyl chloride into an aqueous solution of sodium sulfanilate which had been made alkaline; but, being convinced that this reaction does not proceed smoothly, we ran a condensation by trituration, without dilution by solvents, of a mixture of the two components at the temperature of a water bath. Here there was obtained a very pure benzenesulfonylsulfanilic acid in good yield.

By the action of the sodium salt of this acid on solutions of the chlorides of 2-nitro-, 3-nitro-, 4-nitro- and 2,5-dichlorophenyldiazonium compounds in mineral acids there were prepared four substances, of which three had been described by Schroeter while the fourth was prepared for the first time. The derivative of 2-nitrophenyldiazonium compound, after recrystallization from water, turned out to have an orange color, that from 3-nitrophenyldiazonium compound was light yellow, that from 4-nitrophenyldiazonium compound was egg-yellow, and that from 2,5-dichlorophenyldiazonium compound was lemon yellow. All these under the microscope showed the form of elongated plates. The products are poorly soluble in cold water, while 2-nitrophenyl derivative dissolved best in hot water, while 4-nitrophenyl derivative was less soluble, and the remaining two compounds were even less soluble. All these compounds, according to our experiments, couple quantitatively in neutral medium with azo components and are therefore true diazo salts. They lose the diazo nitrogen quantitatively on being boiled both in acid and in neutral media. In potentiometric titration they behave like true diazonium arylsulfonates since for the 4-nitrophenyldiazonium salt the isoelectric point lies at pH 5.9, while that for 2-nitrophenyldiazonium salt is at pH 4.8, and that for the sodium salt of benzenesulfonylsulfanilic acid is at pH 6.9. It should be noted that Schroeter's assertion to the effect that 4-nitrophenyldiazonium compound forms an azo dye with benzenesulfonylsulfanilic acid, and not a diazonium salt, is evidently based on a misunderstanding.

The table illustrates the dependence of the color of the diazonium salt on the anion of arylsulfamido- or acylaminoarylsulfonic acid which enters its composition.

Dependence of Color of Diazonium Salt on Anion Structure

Diazo cation	Structure of the anion and color of the salt		
			
	Orange	Light yellow	Light yellow-red
	Dark red-brown	Egg-yellow	Greenish-red
	Very dark (red-brown) (very soluble)	Orange	Dark red
	Bright red	Lemon yellow	

From the data in the table it is possible to make the following observations.

1) The benzenesulfonylsulfanilates are considerably more colored than are the analogous arylsulfamates. The cause for the hypsochromic effect is evidently the fact that between the amino and the sulfo groups in benzenesulfonylsulfanilates there is located a phenyl nucleus and that the amino group is replaced by the electrophilic acyl residue.

2) Diazonium acetylnaphthionates are more deeply colored than are the corresponding benzenesulfonylsulfanilates. This bathochromic effect must be explained by the decrease of acidity of the acyl substituent in the amino group and replacement of the phenyl nucleus by naphthalene.

3) In all three series of the colored diazonium salts it is clearly evident that their color deepens within each series from 3-nitro, through 4-nitro, to the 2-nitro derivative, i.e., according to the growth of the electrophilic nature of the nitro group depending on its position in the benzene nucleus.

EXPERIMENTAL

Synthesis of benzenesulfonylsulfanilic acid $C_6H_5SO_2NHC_6H_4SO_3H$. Four g of the sodium salt of sulfanilic acid was triturated in a porcelain dish with 5 g of benzenesulfonyl chloride and was gently heated on a sand bath with energetic rubbing. The precipitate, which at first liquefied, then gradually thickened to a solid paste was transferred to a beaker and was stirred with 30 ml of water heated to 72°. The main bulk of the precipitate went into solution. The solution was filtered from the small amount of a white precipitate, chilled in ice and treated with an excess of sulfuric acid. A colorless crystalline precipitate formed immediately. The precipitate was filtered off after chilling with ice; it was then washed with ice water and dried.

Found %: S 19.9. $C_{12}H_{11}O_5NS_2$. Calculated %: S 20.46.

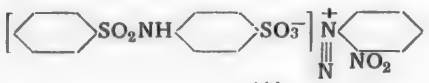
In the potentiometric titration of the benzenesulfonylsulfanilic acid with alkali, its point of equivalence was found at pH 6.9.

Preparation of solutions of the diazo compounds. The arylamine (0.01 mole) was mixed with 6 ml of 5 N hydrochloric acid and stirred for 30 minutes at room temperature, then treated with 7 g of powdered ice whereby the temperature declined to −6°. To this reaction mixture there was added in one portion 2.1 ml of 5 N solution of sodium nitrite. The temperature rose to 6-8° and, after a few minutes, the solution became almost transparent. It was filtered and treated with a few drops of a solution of sulfamic acid for destruction of the excess nitrous acid, controlling the reaction with a test paper dyed with Metanil yellow.

In case of o-nitro- or 2,5-dichloroanilines the amount of the acid was increased to 10 ml and that of nitrite to 2.2 ml.

Reaction of benzenesulfonylsulfanilic acid with diazonium chlorides. Benzenesulfonylsulfanilic acid (0.01 mole) was dissolved in a slight excess of concentrated soda solution. The excess soda was eliminated by addition of acetic acid. To the solution, chilled with ice, there was added with stirring the solution of the diazonium compound prepared from 0.01 mole of amine.

2-Nitrophenyldiazonium salt of benzenesulfonylsulfanilic acid (A). On addition of the diazonium solution into the sulfonate solution there formed immediately a thick yellow-orange precipitate. This was filtered off,



(A)

washed with cold water and recrystallized from water heated to 65-70°. There were obtained crystals with orange color with a golden sheen. Under a microscope they appeared as elongated plates.

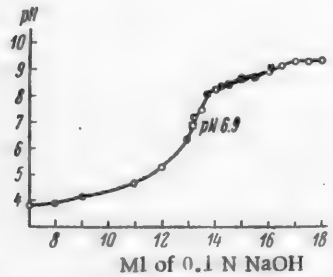


Fig. 1. Potentiometric titration of benzenesulfonylsulfanilic acid.

A solution or a suspension of the substance in water couples intensively with azo dye components. The product is readily soluble, with yellow color, in solutions of sodium hydroxide. A red solution is formed with 20% solution of ammonia, this solution yielding a red precipitate. The substance does not contain sodium (ash).

Analysis for diazo nitrogen content:

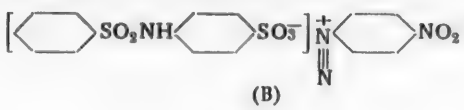
a) Decomposition in 50% sulfuric acid. Found %: diazo nitrogen 6.28. $C_{18}H_{14}O_7N_4S_2$. Calculated %: diazo nitrogen 6.07.

b) Decomposition in boiling water. Found %: diazo nitrogen 5.85. $C_{18}H_{14}O_7N_4S_2$. Calculated %: diazo nitrogen 6.07.

Determination of the diazo component. A sample of the substance was suspended in 150-200 ml of water. To this suspension there was added with good stirring an excess of 0.1 N alkaline solution of β-naphthol, which had been adjusted to pH 7 by addition of acetic acid. After 30-40 minutes stirring the excess β-naphthol was titrated with 4-nitrophenyldiazonium solution. 0.5605 g of substance taken: 12.34 ml of 0.1 N β-naphthol. $C_{18}H_{14}O_7N_4S_2$. Calculated: 12.12 ml of 0.1 N β-naphthol.

In the potentiometric titration of the diazonium salt in aqueous solution with 0.1 N solution of sodium hydroxide the point of equivalence was found to lie at pH 4.

4-Nitrophenyldiazonium salt of benzenesulfonylsulfanilic acid (B). To a concentrated solution



(B)

of the arylsulfonate there was added the diazonium solution. A thick yellow precipitate formed immediately. This was filtered off, washed with cold water and pressed on a porous plate. The diazonium salt was sparingly soluble in cold water, more readily soluble in hot water with formation of a yellowish solution.

No gas evolution was observed on the heating of the aqueous solution to 75°. The diazonium salts coupled energetically with azo dye components. After recrystallization from water at 75° there were obtained, after chilling with ice, the egg-yellow large shiny crystals of the product. Under a microscope these appear as elongated plates.

The substance dissolved in sodium hydroxide with red coloration. In ammonium hydroxide it also gave a red colored solution from which there formed a red-brown precipitate.

Analysis for diazo nitrogen:

Found %: diazo nitrogen 6.23, 6.28. $C_{13}H_{14}O_7N_4S_2$. Calculated %: diazo nitrogen 6.07.

Determination of diazo component (coupling with β-naphthol):

0.6286 g of the substance: 13.5 ml of 0.1 N β-naphthol. $C_{13}H_{14}O_7N_4S_2$. Calculated : 13.59 ml of 0.1 N β-naphthol.

The isoelectric point was found to be at pH 5.9, in the potentiometric titration of the diazo salt with 0.1 N solution of hydrochloric acid with a glass electrode.

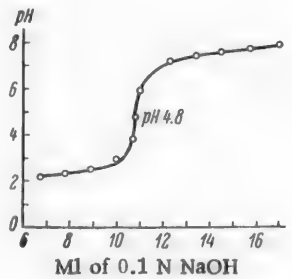


Fig. 2. Potentiometric titration of 2-nitrophenyldiazonium salt of benzenesulfonylsulfanilic acid.

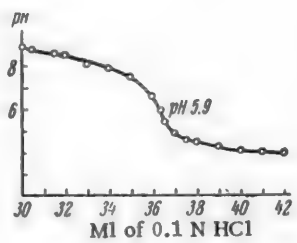
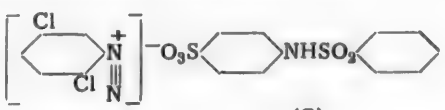


Fig. 3. Potentiometric titration of 4-nitrophenyldiazonium salt of benzenesulfonylsulfanilic acid.

2,5-Dichlorophenyldiazonium salt of benzenesulfonylsulfanilic acid (C). On pouring the diazonium solution into the suspension of benzenesulfonylsulfanilic acid, the reaction mixture crystallized to a thick mass of crystals with lemon yellow color. These appeared as plates under a microscope.



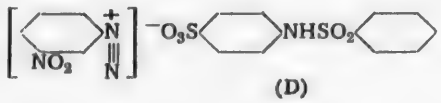
(C)

The precipitate, after filtration, washing and drying, was very slightly soluble in cold water and somewhat more soluble in hot water. The product couples intensively with azo dye components. It dissolved completely with a yellow-orange color in a solution of sodium hydroxide.

Analysis for the content of the diazo component (coupling with β-naphthol):

0.7426 g of product: 14.92 ml of 0.1 N β-naphthol. $C_{18}H_{13}O_8N_5Cl_2S_2$. Calculated: 15.27 ml of 0.1 N β-naphthol.

3-Nitrophenyldiazonium salt of benzenesulfonylsulfanilic acid (D). On mixing the solutions of 3-nitrophenyldiazonium salt and sodium acylsulfanilate there formed immediately a thick yellow precipitate. Under



(D)

the microscope these appeared as slightly yellow plates. The substance was poorly soluble in cold water and somewhat more soluble in hot water. It coupled intensively with azo dye components and formed a yellow solution with sodium hydroxide.

SUMMARY

1. It was shown that the colored reaction products of diazonium salts with acylaminoarylsulfonic acids, which had been synthesized by Schroeter, are true diazonium salts.

2. It was found that diazonium acylaminoarylsulfonates are colored more deeply when the substituents in the aryl nucleus of the diazonium portion are more electrophilic, when the acid character of the acyl group is less pronounced and when a greater number of condensed benzene nuclei are contained in the aryl group of the acylaminoarylsulfonic acid.

3. It was suggested that the reason for the color of the diazonium acylaminoarylsulfonates, as for diazonium arylsulfamates, is the special salt bond between the ions of these salts, which is aided by conjugation between the electron-donor system of the anion and the electrophilic system of the cation.

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SYNTHESES OF VINYL MONOMERS

III. CONCERNING THE SYNTHESES OF VINYL ESTERS FROM ACETO- AND CHLORO-MERCURIACETALDEHYDES AND CONCERNING THE MECHANISM OF THESE REACTIONS

A. Ia. Iakubovich, V. V. Razumovskii, Z. N. Vostrukhina and S. M. Rozenshtein

We decided to use, for the preparation of some vinyl esters, the method of their synthesis that had been described recently by A. M. Sladkov and G. S. Petrov [1]. This method consists of the reaction of acetaldehyde with the chloride of the appropriate acid in the medium of a tertiary base and leads, according to the data given by the authors, to the formation of vinyl ester in yields up to 90% of theoretical.

Working with pyridine we attempted at first to prepare in this manner some vinyl benzoate, using the conditions indicated by the authors to be the optimum ones (yield of ester 83%). However we failed to prepare this ester. Similarly fruitless were the attempts to prepare vinyl acetate by this method. Owing to the briefness of the description of the technique in the cited article, we turned to Sladkov's dissertation [2] and tried to prepare vinyl esters of butyric, caproic and chloroacetic acids, using the detailed directions given in this dissertation. However, none of these esters could be prepared by us, working with pyridine.

It is proper to note here that in the cited publications there are not given any indications that on mixing of pyridine, acetaldehyde and an acyl chloride there occurs an abundant formation of crystalline precipitates; more will be said below about the nature of these compounds.

Vinyl esters of acids of phosphorus may be prepared by the reaction of acetaldehyde with chlorides of such acids in the presence of triethylamine [3]. We made an attempt to prepare some vinyl benzoate with replacement of pyridine by triethylamine. In this case there was obtained some vinyl benzoate in a yield about 15% of theoretical.

Considering the above, we turned to the synthesis of vinyl esters by another method [4]. We prepared by this method in satisfactory yields the vinyl esters of benzoic, p-cyanobenzoic, trifluoroacetic and other acids.

A. N. Nesmeianov and I. F. Lutsenko [5] regard the reactions of monochloromercuriacetaldehyde with acyl chlorides, which leads to the formation of vinyl esters, as reactions with a transfer of the reactive center.

On the basis of material given below it seems to us that such a concept is debatable. In their discussion of the reaction mechanism, Nesmeianov and Lutsenko start with the supposition that carbonyl compounds enter the reactions with acylating agents only with difficulty and that the appearance of a well defined reactivity of the carbonyl group in chloromercuriacetaldehyde in respect to acyl halides is ascribed almost completely to the σ,π-conjugation of the Hg−C and C=O bonds.

However, in reality the carbonyl group of aldehydes in the absence of a conjugated Hg−C bond remains still quite reactive in respect to acyl halides, as will be clear from the data shown below. Actually, according to the data from a number of workers [6-10], benzaldehyde and its derivatives readily add halides of aliphatic and aromatic acids with formation of esters by the reaction scheme:

Formaldehyde also reacts analogously as has been shown by many examples [11, 12] and confirmed in the present work by the syntheses of chloro- and bromomethyl methacrylates from paraformaldehyde and corresponding halides of methacrylic acid.

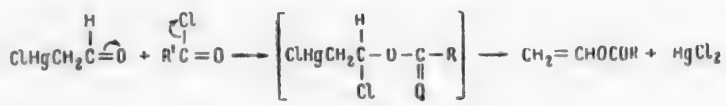
Evidently, the activity of the carbonyl group in formaldehyde is sufficiently great despite the absence of π,π-conjugation of the carbonyl group bond, as it exists in the analogously reacting benzaldehyde and cinnamaldehyde, and the addition of acyl halides to it proceeds easily. However, formaldehyde is not an exception. Acetaldehyde, as established by us in an example with acetyl chloride, is capable of combining with it on simple mixing at normal temperature with heat evolution, forming α-chloroethyl acetate thereby. In the presence of traces of zinc chloride which catalyzes the addition, the reaction proceeds violently.

We prepared the previously undescribed α-chloroethyl methacrylate by the reaction of acetaldehyde with the chloride of methacrylic acid in the presence of zinc chloride. A similar addition has been observed previously [13-16] in heating of a mixture of acetaldehyde or its homologs with acyl chlorides in a sealed tube at 100°. Thus, it is quite clear that the readily proceeding addition of acyl chlorides to aldehydes with formation of α-halogenated alkyl or aralkyl esters of carboxylic acids is a general reaction.*

There is hardly an basis to think that in the case of chloromercuriacetaldehyde its reaction with acyl halides must proceed by another route and to speak in this case about the transfer of the reactive center [18].

The "dual" reactivity of chloromercuriacetaldehyde in respect to acyl halides (incidentally, one never observed thus far) or to compounds analogous to them (triphenylhalomethanes) may arise, evidently owing to the fact that this aldehyde is a bifunctional compound.

Whether the reaction of chloromercuriacetaldehyde with acyl halides yields vinyl esters of the result of elimination of mercuric chloride in two stages, i.e., as a 1-2 addition according to the scheme:



or whether the entire reaction proceeds in one act (1-4 addition), is not strictly proven at this time. However, all the material shown above and below about the reactions of aldehydes with acyl halides permits one to allow that the reaction may proceed in two stages; here as the result of the addition of acyl halide to chloromercuriacetaldehyde there arises an unstable β-chloromercuric chloride which, by losing mercuric chloride, is transformed into the vinyl ester. This possibility is confirmed by some degree by the material shown below.

We isolated and examined the crystalline compounds formed in the reaction of acetaldehyde and pyridine with benzoyl chloride and acetyl chloride. Their examination showed that they are adducts of the composition $(C_5H_5NRCOClCH_3CHO)_x$. By their behavior and properties these compounds are salt-like substances.

The same compounds could be prepared by the reaction of pyridine with α-chloroethyl benzoate and α-chloroethyl acetate, respectively:

$$RCO_2CHClCH_3 + C_5H_5N \longrightarrow \underset{(I)}{[C_5H_5NCH(CH_3)(O_2CR)]Cl}$$

Thus it appears evident that the adducts are salts of quaternary bases, i.e., chlorides of α-acyl(aroyl)hydroxyethylpyridinium ion (I) (also see [10]).

We also found that in the reaction of acetaldehyde, benzoyl chloride and triethyl amine there is formed in 15% yield some vinyl benzoate. One can hardly doubt that in this reaction, as well, there occurs the intermediate formation of a quaternary salt which is analogous to those shown above. However this salt, being less stable thermally than the corresponding pyridinium salt, decomposes already at room temperature, forming thereby the vinyl benzoate along with other substances:

$$(C_2H_5)_3N + C_6H_5COCl \longrightarrow (C_2H_5)_3NC_6H_5COCl \xrightarrow{CH_3CHO}$$

$$\longrightarrow [(C_2H_5)_3NCH(CH_3)(O_2CC_6H_5)]Cl \longrightarrow (C_2H_5)_3NHCl + CH_2{=}CHOCOC_6H_5$$

*Formation of analogous esters in the reaction of aldehydes with chlorides of acids of phosphorus has been noted by M. I. Kabachnik and E. S. Shepeleva [17].

This concept of the course of this reaction is confirmed by the results of the thermal decomposition of the chloride of α-benzoxyethylpyridinium ion, studied by us. The substance decomposes at 185-190°, forming vinyl benzoate in about 20% yield.*

If the above shown scheme for the formation of vinyl ester from acetaldehyde and an acyl chloride in triethylamine medium correctly shows the reaction mechanism for this reaction, as one may admit from all the material discussed above, then one should consider that the nature of the origin of vinyl ester groupings in this reaction and in the Nesmeianov reaction is common to each other. In one case there occurs an α,β-dehydrohalogenation of α-chloroethyl ester as the result of a Hoffman decomposition of the quaternary ammonium salt, while in the other case there occurs a α,β-dechloromercuration of a β-mercury substituted α-chloroethyl ester of the acid.

EXPERIMENTAL

I. Addition Reactions of Acyl Halides to Aldehydes

Preparation of chloromethyl methacrylate. To a mixture of 52.3 g of methacrylyl chloride and 15 g of paraformaldehyde there was added a 60-65° 1.5 g of anhydrous zinc chloride; the mixture began to boil. After clarification, the mixture was distilled in vacuum and the fraction at 70-110° at 15 mm was collected. The distillate was kept for two days over fused potassium carbonate and was then fractionated. There was obtained 25.1 g (36%) of chloromethyl methacrylate:

B.p. 63-65° at 62 mm, d^{20}_4 1.1346, $n^{20}D$ 1.1449;** MR_D 31.5; calculated 31.3.
Found %: C 44.70; H 5.25; Cl 25.53. $C_5H_7O_2Cl$. Calculated %: C 44.6; H 5.20; Cl 26.3.

Preparation of bromomethyl methacrylate. After termination of the reaction of 75 g of methacrylyl bromide and 15 g of paraformaldehyde (2.0 g anhydrous zinc chloride) under the conditions of the previous experiment, the filtrate was freed of unreacted bromide by means of a benzene solution of aniline (20 g of aniline in 150 ml). The precipitate was filtered off and the filtrate was washed with 3% hydrochloric acid, and with water, then was dried and distilled in the presence of cuprous chloride; there was collected a fraction with b.p. 60-90° at 50 mm (58 g). After a second fractionation there was isolated 32 g (35.8%) of bromomethyl methacrylate:

B.p. 85-86° at 50 mm, d^{20}_4 1.4173, $n^{20}D$ 1.4690, MR_D 34.6; calculated 34.24.
Found %: C 33.41; H 3.66; Br 44.52. $C_5H_7O_2Br$. Calculated %: C 33.5; H 3.9; Br 44.7.

Preparation of α-chloroethyl acetate. To 46 g of acetyl chloride there was rapidly added 35 g of acetaldehyde (heating of the mixture was observed) and the mixture was stirred for three hours. After distillation there were collected two fractions: 40-100° (37.3 g) and 101-125° (42.5 g). After a second distillation there was obtained 32.2 g of the α-chloroethyl acetate for 43.8% yield, from the fraction 101-125°.

B.p. 120-124°, d^{20}_4 1.108, $n^{20}D$ 1.4080 (according to data of [19]: b.p. 120-124°).
Found %: Cl 28.8. $C_4H_7O_2Cl$. Calculated %: Cl 28.9.

Preparation of α-chloroethyl methacrylate. To the mixture of 104 g of methacrylyl chloride and 52 g of acetaldehyde preheated to 40° there was added a pair of small pieces of anhydrous zinc chloride (violent reaction). The mixture was stirred for one hour at 50° with 0.1 g of cuprous chloride. Two fractions were collected on distillation: 40-45° at 3 mm, 109 g, and 46-70° at 3 mm, 12 g. On second distillation of the first fraction there was isolated 105 g of α-chloroethyl methacrylate (70.7%).

B.p. 41-42° at 3 mm, d^{20}_4 1.0801, $n^{20}D$ 1.4386, MR_D 36.14; calculated 35.96.
Found %: C 49.48, 49.63; H 6.97, 6.87; Cl 24.32. $C_6H_9O_2Cl$. Calculated %: C 48.5; H 6.1; Cl 23.9.

Preparation of α-chloroethyl benzoate. To the mixture of 140 g of benzoyl chloride and 80 g of acetaldehyde there was added 0.1 g of anhydrous zinc chloride (energetic reaction). The mixture, heated to 70-75°, was kept for 1 hour; then 150 ml of ether was added and the solution was washed with 10% solution of sodium carbonate. After the usual treatment and triple distillation of the product there was obtained 77.5 g (42%) of α-chloroethyl benzoate:

B.p. 97-98° at 1 mm, d^{20}_4 1.172, $n^{20}D$ 1.5171. According to data of [16]: b.p. 120° at 8 mm.

* An analogous conception of the mechanism of formation of vinyl esters in the reaction of acetaldehyde, chlorides of acids and phosphorus and tertiary bases, was expressed by Gefter [3].
** As in original – Publisher's note.

Found %: Cl 19.1. $C_9H_9O_2Cl$. Calculated %: Cl 19.2.

II. Reaction of Acetaldehyde With Halides of Acids in the Presence of Tertiary Bases

Acetaldehyde of acyl chlorides were used in the freshly distilled state. Pyridine was dried over potassium hydroxide and was then distilled from barium oxide, the fraction 115.5-116.1° being collected.

Preparation of α-benzoxyethylpyridinium chloride. a) To the solution of 27 g of acetaldehyde in 95 g of pyridine there was added over 2.5 hours at −10° to −12° with stirring 42 g of benzoyl chloride, during which the formation of a crystalline precipitate was observed.

The precipitate was filtered off and washed with dry ether. The yield was 76 g (96.3%, calculated on benzoyl chloride). The substance is readily soluble in water and the solution gives a test for chloride ion. It is soluble in alcohol, chloroform and glacial acetic acid and insoluble in ether and benzene. It was recrystallized from alcohol by addition of four volumes of ether; it formed colorless needles melting with decomposition at 179-180°.

Found %: C 63.80, 63.60; H 5.04, 5.22; N 5.16, 5.22; Cl 13.28, 13.32. M 532.5 (cryoscopic; acetic acid), 534.0 (ebullioscopic; chloroform). $(C_{14}H_{14}O_2NCl)_2$. Calculated %: C 63.75; H 5.31; N 5.31; Cl 13.43. M 527.

b) A mixture of 23 g of α-chloroethyl benzoate and 12 g of dry pyridine was heated for five hours at 80°. On the following day the upper liquid layer was decanted and the resulting glassy resinous product was washed three times with dry ether. On rubbing with a glass rod, the product crystallized. The yield was 5.7 g. On the following day, from the reaction liquid there separated 2.3 g of additional crystals of the same product. The substance was recrystallized from alcohol by precipitation with ether; it formed colorless crystals which decomposed at 173-175°.

Found %: C 62.94, 62.83; H 5.55, 5.83; N 4.58, 4.78; Cl 13.9, 13.5. $C_{14}H_{14}O_2NCl$. Calculated %: C 63.75; H 5.31; Cl 13.43; N 5.31.

Preparation of α-acetoxyethylpyridinium chloride. a) To a mixture of 55 g of pyridine and 13.5 g of acetaldehyde there was added a 0° with stirring 11.7 g of acetyl chloride, the addition being made gradually; formation of a precipitate began shortly. After heating the mixture to 80° the further treatment was as in the previous experiment. The yield was 35 g (83.3% , calculated on acetyl chloride). The substance dissolves in water, alcohol and chloroform and is insoluble in ether. It was recrystallized from alcohol by precipitation with ether. Colorless crystals with m.p. 140-150° (with decomposition).

Found %: C 52.36, 52.50; H 7.25, 7.40; N 7.61, 7.73. $C_9H_{12}O_2NCl$. Calculated %: C 53.20; H 6.0; N 6.95.

b) A mixture of 40 g of pyridine and 19 g of α-chloroethyl acetate was stirred for five hours while the temperature was gradually raised to 80°. The resulting precipitate was filtered off, washed with absolute ether and dried. The yield was 28.5 g (54%). The substance was recrystallized from alcohol by precipitation with ether; colorless needles with m.p. 140-150° (with decomposition).

Found %: C 53.64; H 6.5; N 7.17; Cl 18.67. $C_9H_{12}O_2NCl$. Calculated %: C 53.2; H 6.0; N 6.95; Cl 17.6.

Preparation of vinyl benzoate. a) To 81 g of triethylamine there was added a mixture of 28 g of benzoyl chloride and 17.6 g of acetaldehyde. The mixture was stirred for four hours at room temperature and stood for 48 hours. The resulting precipitate of triethylamine hydrochloride was separated. After two distillations of the filtrate there was isolated 12 g of a liquid with b.p. 51-53° at 2-3 mm which was not separated by further fractionation. According to chlorine analysis this liquid contained 32% of benzoyl chloride. To the solution of 10 g of this liquid in 75 ml of benzene there was added, for the separation of benzoyl chloride, gradually 4.6 g of aniline in 75 ml of benzene. The precipitate of benzanilide (7.1 g) was filtered off. The filtrate was washed with 0.5 N sulfuric acid and water, dried and subjected to vacuum distillation. There was isolated 4 g (16% on benzoyl chloride) and vinyl benzoate with b.p. 63-63° at 2-3 mm, d^{20}_4 1.0670, $n^{20}D$ 1.5270.

A specially prepared mixture of vinyl benzoate and benzoyl chloride in 2:1 weight ratio boiled without separation at 50° at 2-3 mm.

b) 26.5 g of α-benzoxyethylpyridinium chloride was heated in a flask at 1-2 mm pressure on an oil bath at

187-190°. In a trap which was cooled with dry ice there was collected 0.5 g of a liquid, on the distillation of which there were detected pyridine and acetaldehyde. In the receiver after the trap, there was collected 6.5 g of a liquid. An ethereal solution of this liquid was washed with 0.5 N solution of hydrochloric acid, and with water; after drying it was distilled yielding 3.3 g (20%) of vinyl benzoate with b.p. 80-81° at 6-7 mm, $n^{20}D$ 1.5260.

III. Syntheses of Vinyl Esters by the Nesmianov Method

Preparation of vinyl p-cyanobenzoate was run by the technique which was described for vinyl p-nitrobenzoate [4].

From 12.5 g of chloromercuriacetaldehyde and 6.5 g of p-cyanobenzoyl chloride there was obtained 5.2 g of a crystalline substance with m.p. 46-47°. After recrystallization from anhydrous alcohol (10 g of alcohol per 1 g of product) with chilling of the solution to −70° there was obtained 3.5 g (50%) of vinyl p-cyanobenzoate with m.p. 44-45°.

Found %: C 68.64, 68.51; H 4.57, 4.75; N 7.79, 8.17. $C_{10}H_7O_2N$. Calculated %: C 69.36; H 4.04; N 8.09.

Preparation of vinyl trifluoroacetate. Into a mixture of 35 ml of dry xylene and 28 g of monochloromercuriacetaldehyde there was passed with stirring at 4-5° 10 g of trifluoroacetyl chloride over five hours. Then the mixture was stirred for one hour at room temperature and allowed to stand until the next day. The precipitate was filtered off and the reaction product was distilled from the solution of 50° at pressure of 30 mm, the product being collected in a receiver cooled with a mixture of dry ice and acetone. The distillate (6 g) was kept for three days over solid sodium bicarbonate and was then distilled. After a second distillation there was collected 4.5 g (32%) of vinyl trifluoroacetate with b.p. 40-41°, $n^{25}D$ 1.3210. According to patents [20]: b.p. 37-39° and 40.5°, $n^{24}D$ 1.3162, and $n^{25}D$ 1.3151.

SUMMARY

1. It was impossible to reproduce the synthesis of a series of vinyl esters of carboxylic acids from acetaldehyde, acyl chlorides and pyridine. In these reactions there were isolated the α-acyloxyalkylpyridinium chlorides, which were stable compounds. Vinyl benzoate was obtained in 15% yield of the theoretical after replacement of pyridine by triethylamine in the reaction with benzoyl chloride.

2. By direct addition of acyl halides to aldehydes there were synthesized α-chloroethyl acetate, α-chloroethyl benzoate, chloromethyl methacrylate, bromomethyl methacrylate and α-chloroethyl methacrylate. The reaction of addition of acyl halides to aldehydes is a completely general one and deserves mention in manuals on organic chemistry along with other typical reactions of addition among aldehydes.

3. By means of Nesmeianov reaction (Nesmeianov and co-workers) – reaction of monochloromercuriacetaldehyde with acyl halides – there were synthesized vinyl trifluoroacetate and vinyl p-cyanobenzoate.

The chemistry of the Nesmeianov reaction and the reaction of formation of vinyl benzoate from acetaldehyde and benzoyl chloride were discussed.

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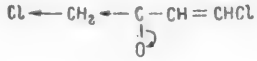
* In Russian.

A STUDY IN THE ISOXAZOLE SERIES

VI. CONCERNING THE SYNTHESIS OF 3-SUBSTITUTED ISOXAZOLES

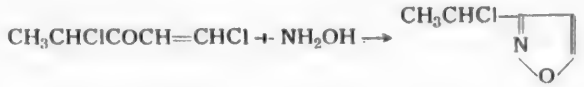
N. K. Kochetkov and A. Ia. Khorlin

One of the simplest methods of synthesis of isoxazole – the reaction of β-chlorovinyl ketones with hydroxylamine – has been studied in detail in our laboratory [1, 2]. A material fault of this method is the formation of a mixture of approximately equal amounts of isomeric 3- and 5-substituted isoxazoles, which fact is due to the two competing processes – the nucleophilic attack of hydroxylamine at the oxygen of the carbonyl group or at the β-carbon atom with replacement of the chlorine atom [1]. It was later shown by one of us [3] that β-dialkylaminovinyl ketones react with hydroxylamine in a practically singular manner, forming almost pure 5-substituted isoxazoles; in this case the attack of hydroxylamine is directed to the β-carbon atom owing to the suppression of the electrophilic activity of the carbonyl group. Finally it was shown [1] that chloromethyl β-chlorovinyl ketone reacts and forms 3-chloromethylisoxazole. This latter circumstance indicates that in this case the nucleophilic attack by hydroxylamine is directed solely at the carbonyl group, which is distinguished by an enhanced electrophilicity, evidently owing to the additional inductive effect produced by the halogen atom in α'-position.

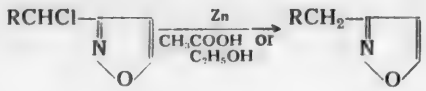


For checking this supposition we decided to establish whether or not such an effect of the halogen atom is general for the α'-position of the alkyl radical of alkyl β-chlorovinyl ketones and, with this purpose in mind, we studied the reaction of α'-chloroethyl β-chlorovinyl ketone with hydroxylamine.

Only chloromethyl β-chlorovinyl ketone and β'-chloroethyl β-chlorovinyl ketone are known at this time among alkyl β-chlorovinyl ketones which have substituents in the alkyl radical. It turned out that the synthesis of α'-chloroethyl β-chlorovinyl ketone also does not present any difficulties and is readily performed by the general method of synthesis of alkyl β-chlorovinyl ketones developed in our laboratory [4]. In the condensation of α'-chloroethyl β-chlorovinyl ketone with hydroxylamine in methanol there was obtained, in good yield, α'-chloroethyl isoxazole, which did not give a precipitate after treatment with sodium alcoholate according to Claisen [5]. This fact indicated that the isoxazole prepared by us is indeed the 3-substituted isomer.



In order to solve more definitely the question of the degree of purity of the 3-substituted isomers prepared by us in the cases of 3-α'-chloroethylisoxazole and the previously described 3-chloromethylisoxazole, we accomplished the reduction of these α'-chloroalkylisoxazoles into the corresponding alkylisoxazoles and studied the compounds obtained thusly from the point of view of possible presence in them of admixtures of the 5-substituted isomers. The α'-chloroalkylisoxazoles are reduced smoothly to the corresponding alkylisoxazoles by means of zinc dust in acetic acid or alcohol.



The cleavage of the resulting methyl- and ethylisoxazoles by sodium alcoholate according to Claisen [5] showed that methylisoxazole contained 10% and ethylisoxazole contained 3% of the 5-substituted isomer. Since the absence of isomerization of the 3-substituted isomer under the conditions of reduction was confirmed by a special experiment, the above result makes us admit that the reaction of chloromethyl β-chlorovinyl ketone with hydroxylamine does not proceed completely in a single path, as it had been indicated by us previously [1, 6]. At the same time this shows that the predominant direction of the reaction of α'-chloroalkyl β-chlorovinyl ketones with hydroxylamine is still the formation of the 3-substituted isoxazole, which fact confirms the thought, expressed in the first part of this paper, about the material effect of the chlorine atom in α'-position in the alkyl residue in β-chlorovinyl ketones on the direction of reaction with hydroxylamine.

In conclusion it should be mentioned that despite the lack of specificity in the course of the reaction of α'-chloroalkyl β-chlorovinyl ketones with hydroxylamines, this reaction is still at the present time the best method for a directed synthesis of 3-substituted isoxazoles insofar as all the existing methods of synthesis always yield a mixture of 3- and 5-substituted isomers. The method of reduction of α'-chloroalkylisoxazoles, developed by us, makes accessible the pure 3-alkylisoxazoles.

EXPERIMENTAL

α-Chloropropionyl chloride was prepared by chlorination of propionyl chloride with sulfuryl chloride by the Kharash method [7], with modifications which had been described by us previously [8]. The yield was 60%; b.p. 109-111°.

α'-Chloroethyl β-chlorovinyl ketone. Into a three-necked flask provided with a stirrer, a reflux condenser, a gas inlet tube and a thermometer, there was placed a solution of 28.6 g of α-chloropropionyl chloride in 80 ml of carbon tetrachloride. A not too energetic stream of acetylene was passed through the solution while over one hour at 15-20°, with stirring, there was added 29.5 g of anhydrous aluminum chloride in small portions. The acetylene was introduced at this temperature for four hours longer. Then the reaction mixture was poured on ice, the layer of carbon tetrachloride was separated, the aqueous layer was extracted with ether and the combined extracts and the main portion of the product were dried over magnesium sulfate. The α'-chloroethyl β-chlorovinyl ketone was isolated by distillation. The yield was 19.5 g (55%); b.p. 69-70° at 11 mm.

$n^{20}D$ 1.4960, d^{20}_4 1.2640, MR_D 35.36; calculated 34.57; EMR_D 0.79.
Found %: C 39.49, 39.19; H 4.18, 4.31. $C_5H_6OCl_2$. Calculated %: C 39.25; H 3.95.

The ketone was a colorless oily liquid with a characteristically sharp odor; it was a strong lachrymator. It darkens rapidly in storage, but can be preserved for a long time in the cold in ether solution.

3-α'-Chloroethylisoxazole. To the solution of 12.7 g of hydroxylamine hydrochloride in 70 ml of methanol there was added 20.0 g of α'-chloroethyl β-chlorovinyl ketone. After six hours of refluxing the mixture was poured into 250 ml of water and extracted several times with ether; the extracts were dried over magnesium sulfate, the solvent was distilled and the residue was distilled, collecting the fraction with b.p. 69-70° at 20 mm. The yield was 14.6 g (86%).

$n^{20}D$ 1.4729, d^{20}_4 1.1869, MR_D 30.28; calculated 30.87.*
Found %: N 10.62, 10.53. C_5H_6ONCl. Calculated %: N 10.64.

The substance is a colorless oil with a characteristic odor. It is a weak lachrymator.

Reduction of 3-chloromethylisoxazole. 1. To the solution of 36.5 g of 3-chloromethylisoxazole in 200 ml of 90% alcohol there was added with stirring 100 g of zinc dust. After refluxing for 1.5 hours, the precipitate was filtered off, washed on the filter with 50 ml of alcohol and to the hot mother liquor there was added a hot saturated solution of 100 g of cadmium chloride in water. The precipitate of the cadmium complex of methylisoxazole,

* The increment of nitrogen in the ring was taken as 2.84 in the paper [1].

which formed after one day, was filtered off and washed on the filter with 50 ml of cold saturated solution of cadmium chloride. The methylisoxazole was isolated by decomposing the cadmium complex as described earlier [1]. There was obtained 15.3 g of the product (58%) with b.p. 117.5-119° at 750 mm.

$n^{20}D$ 1.4345, d^{20}_4 1.0189, MR_D 21.27; calculated 21.39.

According to literature data for 3-methylisoxazole [5]: b.p. 118.5°, $n^{20}He$ 1.4345, d^{20}_4 1.022; according to data [1]: b.p. 118°, $n^{20}D$ 1.4345, d^{20}_4 1.0206; for 5-methylisoxazole according to data [3]: b.p. 121-122°, $n^{20}D$ 1.4368, d^{20}_4 1.0224.

The determination of the content of the α-isomer in the methylisoxazole was performed as described previously [1]. After treatment of 2.97 g of methylisoxazole with sodium ethoxide (from 1.0 g of sodium) in 90 ml of anhydrous ethanol, there was obtained 0.410 g of sodiocyanoacetone, which corresponded to the content of 11% of 5-methylisoxazole. Phenylhydrazone of cyanoacetone has m.p. 100-101° (from alcohol).

According to data [9], m.p. 101-102°; according to data [1], m.p. 100°.

2. To the solution of 23.5 g of 3-chloromethylisoxazole in 100 ml of glacial acetic acid there was added with stirring 30.0 g of zinc dust, the temperature being maintained at not above 70°. After termination of the self-heating of the reaction mixture (3 hours), the mixture was heated on a boiling water bath for one hour. Then the precipitate was filtered off, washed on the filter with 20 ml of glacial acetic acid and the mother liquor was diluted with 300 ml of water, carefully neutralized with sodium carbonate and extracted several times with ether. The ethereal extracts were dried over magnesium sulfate, the ether was distilled from a flask with a 75 cm fractionating column, and the residue was distilled, collecting the fraction with b.p. 118-122° at 750 mm. The yield was 9.7 g (59%).

$n^{20}D$ 1.4360, d^{20}_4 1.0202, MR_D 21.23; calculated 21.39.

By the action of sodium ethoxide there was obtained from 2.235 g of methylisoxazole, by the above method, 0.285 g of sodiocyanoacetone (indicative of 10% of 5-methylisoxazole); phenylhydrazone of cyanoacetone had m.p. 99° (from alcohol).

Reduction of 3-α'-chloroethylisoxazole was run in glacial acetic acid analogously to the one described above. From 7.0 g of chloroethylisoxazole and 5.4 g of zinc dust in 25 ml of glacial acetic acid there was obtained 2.5 g (54%) of ethylisoxazole.

B.p. 137-139° at 740 mm, $n^{20}D$ 1.4370, d^{20}_4 0.9874, MR_D 25.80; calculated 26.00.

For a mixture of 5-ethylisoxazoles, according to [1]: b.p. 139-140°, $n^{20}D$ 1.4440, d^{20}_4 0.9916.

From 1.015 g of ethylisoxazole and sodium ethoxide there was obtained 0.037 g (3% of 5-α'-ethylisoxazole) of sodio-1-cyano-2-butanone. Phenylhydrazone of 1-cyano-2-butanone had m.p. 87-88° (from alcohol). For phenylhydrazone of 1-cyanobutanone according to [1]: m.p. 88-89°.

SUMMARY

1. It was shown that α'-chloroalkyl β-chlorovinyl ketones react with hydroxylamine with formation of 3-α'-chloroalkylisoxazoles with a small admixture of 5-substituted isomers.

2. A method of preparation of 3-alkylisoxazoles was developed by the reduction of the corresponding 3-α'-chloroalkylisoxazoles with zinc dust.

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A STUDY IN THE FIELD OF THIOSULFONIC ACIDS

IV. CONCERNING THE MECHANISM OF THE REACTION OF FORMATION OF THIOSULFONATES

B. G. Boldyrev and T. A. Trofimova

Alkane- and arenethiosulfonic acids may be prepared in the form of salts RSO_2SM (I) by the action of halides of sulfonic acids on aqueous solutions of potassium hydrosulfide [1-4].

Owing to the fact that in the process of the reaction there occurs a separation of elemental sulfur, which on further heating of the reaction mixture goes into solution, it is supposed [2, 3] that the formation of thiosulfonates (I) proceeds according to the following general scheme of reactions:

$$RSO_2Cl + K_2S \longrightarrow RSO_2K + KCl + S, \quad (1)$$

$$RSO_2K + S \longrightarrow RSO_2SK. \quad (2)$$

Specifically in this manner did Blomstrand [1] prepare and isolate for the first time the potassium salt of p-toluenethiosulfonic acid, without discussing the mechanism of the reaction itself at that time.

Later, Spring [2] repeated Blomstrand's experiments with the example of preparation of benzenethiosulfonate and expressed the supposition that the reaction proceeds through a stage of formation of a salt of sulfinic acid. He also reported that he was able to prepare the same product by the reaction of a salt of benzenesulfinic acid with sulfur and to isolate from the reaction mixture a salt of sulfinic acid. The author, however, did not cite the technique of the experiments nor did he give the proofs of identity of the products obtained by the various routes.

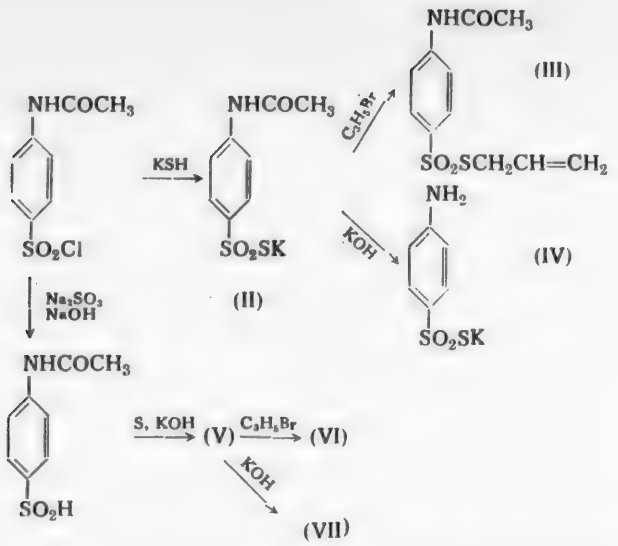
For this reason we considered it interesting to check in this work the correctness of the previously suggested concepts about the mechanism of the reaction of formation of thiosulfonates, especially since this method specifically – reaction of sulfonyl chlorides with potassium hydrosulfide – had been used previously [5-9] for the preparation and isolation of over twenty salts of various thiosulfonic acids.

The possibility of formation of thiosulfonates according to reaction (2) was decided to be tested by us with the example of preparation of the potassium salt of acetylthiosulfanilic acid (II). For this purpose p-acetylaminobenzenesulfonyl chloride was converted, by the reaction with an aqueous solution of potassium hydrosulfide, into thiosulfonate (II). By the usual method [10] from the same chloride there was prepared the p-acetylaminobenzenesulfinic acid; by heating the alkaline solution of its potassium salt with elemental sulfur we obtained product (V), the identification of which was made by the scheme shown below.*

The products of the reactions (II) and (V) isolated by us turned out to be completely identical with each other: they were colorless crystalline substances with m.p. 256°; no depression was found in their mixed melting point.

Completely identical also were their derivatives – allyl esters (III) and (VI), as well as the products of deacetylation – potassium salts of [(IV) and (VII)] thiosulfanilic acid.

*Substances (II-IV) were first prepared by M. A. Belous [11].



Thus, the supposition expressed previously by other authors that the salts of thiosulfonic acids may be synthesized by the reaction of salts of sulfinic acids with elemental sulfur [2], was completely confirmed.

This fact, however, does not speak as yet about the fact that the preparation of thiosulfonates (I) from chlorides of sulfonic acids and hydrosulfides of alkali metals proceeds through the stage of formation of salts of sulfinic acids.

In order to confirm the mechanism of this reaction one should isolate potassium sulfinate directly from the reaction mixture after the preparation of the thiosulfonate (II) before the solution of the elemental sulfur which formed during the reaction.

Our first attempts to isolate the sulfinate from such a reaction mixture ended in failure since even at low temperature the potassium sulfinate reacted readily with elemental sulfur with formation of the thiosulfonate, which fact hindered the isolation of small amounts of the salt of the sulfinic acid remaining in the solution.

However, by running the reaction with a dilute solution of potassium hydrosulfide at −2° it turned out to be possible to retard to a considerable degree the secondary reaction of formation of the thiosulfonate and to isolate from the reaction mixture some p-acetylaminobenzenesulfinic acid which was then identified by its conversion to the thiosulfonate (II) and then into the allyl ester (III) of acetylthiosulfanilic acid.

This confirmed that the preparation of thiosulfonates (II) by the reaction of halides of sulfonic acids with hydrosulfides of alkali metals actually does proceed through the intermediate stage of formation of salts of sulfinic acids.

EXPERIMENTAL

The starting materials for the syntheses of thiosulfonate (II) – chloride of acetylsulfanilic acid and p-acetylaminobenzenesulfinic acid – were prepared by us through the usual paths [12, 10].

Preparation of potassium acetylthiosulfanilate. a) From the chloride of acetylsulfanilic acid and potassium hydrosulfide. This synthesis was run by us under conditions described previously [7, 8] for other thiosulfonates. Here from 280 g of the chloride of acetylsulfanilic acid and potassium hydrosulfide prepared by saturation with hydrogen sulfide of a solution of 150 g of potassium hydroxide in 300 ml of water, there was prepared 215 g (70%) of colorless crystalline substance with m.p. 256°. The product was readily soluble in water and boiling alcohol; it was insoluble in benzene, ether, acetone and chloroform; it crystallized from alcohol in the form of reactangular plates.

Found %: S 23.70, 23.67. $C_8H_8O_3NS_2K$. Calculated %: S 23.81.

b) From potassium p-acetylaminobenzenesulfinate and elemental sulfur. p-Acetylaminobenzenesulfinic acid (26.5 g) was dissolved in an excess* of 30% solution of potassium hydroxide (10.2 g in 26 ml of water) and heated with 4.3 g of thoroughly powdered elemental sulfur on a boiling water bath for 2.5 hours. After the heating the sulfur was almost completely dissolved and the solution had a reddish-orange color, characteristic of polysulfides. After addition of charcoal and filtration, the solution was evaporated to dryness on a water bath and the dry residue was extracted with alcohol and the resulting crystalline product was recrystallized from the same solvent.

The yield of colorless thiosulfonate with m.p. 256° was 22.2 g (63.2%).

Found %: S 23.52, 23.48. $C_8H_8O_3NS_2K$. Calculated %: S 23.81.

The mixed melting point of this product with the acetylthiosulfanilate prepared by Method a showed no depression.

Preparation of allyl ester of acetylthiosulfanilic acid. The allyl ester (III) was synthesized by us by the reaction of potassium acetylthiosulfanilate with allyl bromide in aqueous acetone solution by the method described for the preparation of analogous esters of other thiosulfonic acids [4]. Here from 15.0 g of potassium salt and 6.8 g of allyl bromide there was obtained 9.9 g (66.6%) of allyl ester (III).

After recrystallization from 40% alcohol the product appeared as a colorless crystalline substance with m.p. 59-60°. It was poorly soluble in water, excellently soluble in alcohol, ether, acetone and other organic solvents; it crystallized from 40% alcohol in the form of crystals having the shape of triangular prisms.

Found %: S 23.55. $C_{11}H_{13}O_3NS_2$. Calculated %: S 23.63.

The same ester was prepared by an analogous route from product (V); the mixed melting point of the esters showed no depression.

Preparation of potassium thiosulfanilate. Potassium acetylthiosulfanilate (76.5 g) was introduced into 170 ml of 10% solution of potassium hydroxide and was heated for two hours on a boiling water bath with mechanical stirring. Then to the resulting orange solution under the same conditions there was added dropwise 10% acetic acid until the mixture became neutral to phenolphthalein. After addition of some activated charcoal and a ten-minute standing, the solution was filtered and from the filtrate on cooling there precipitated the colorless crystals of potassium thiosulfanilate. The product was filtered off and washed with alcohol, and the filtrate was concentrated to half the original volume after which from it precipitated an additional considerable amount of the same product. After two recrystallizations from alcohol there was obtained the colorless crystalline substance with m.p. 237-238° (with decomposition). The yield of the salt was 41.0 g (63.7%).

Potassium thiosulfanilate was readily soluble in water and boiling alcohol; it was insoluble in ether, benzene, chloroform and acetone; it crystallized from alcohol in the form of thin needles.

Found %: S 28.11. $C_6H_6O_2NS_2K$. Calculated %: S 28.21.

The deacetylation of product (V) was run in analogous manner. The mixed melting point of the thiosulfonates showed no depression.

Isolation of p-acetylaminobenzenesulfinic acid from the reaction mixture in the preparation of acetylthiosulfanilate. The solution of 30 g of potassium hydroxide in 60 ml of water was saturated with hydrogen sulfide and diluted with 4 parts of water; then at the temperature of −2° with mechanical stirring there was added to it 60 g of previously recrystallized chloride of acetylsulfanilic acid. The resulting precipitate of sulfur was filtered off and to the dark green solution there was added concentrated sulfuric acid until the filtrate became colorless. Then the filtrate was chilled with a mixture of ice and salt and to it there was added an excess of acid until a

*In case of equimolar amount of alkali the reaction between the sulfinate and the sulfur proceeds extremely slowly; it is possible that the formation of potassium polysulfides aids the more energetic course of the main reaction of formation of the salt of thiosulfonic acid. In the preparation of benzenethiosulfonate by the same method the reaction proceeds smoothly and without excess of alkali even in the case in which one uses a previously prepared salt of benzenesulfinic acid; it is true that in this case the medium shows an alkaline reaction and hence it is possible to admit the formation of small amounts of polysulfides.

colorless crystalline precipitate formed. After recrystallization from water there was obtained 9.52 g (19.2%) of product with m.p. 151-153°.

Found %: S 16.29, 16.11. $C_9H_9O_3NS$. Calculated %: S 16.10.

The mixed melting point of the isolated product with the sulfinic acid prepared by the usual route showed no depression.

The identification of p-acetylaminobenzenesulfinic acid was made by its transformation into the thiosulfonate by heating with sulfur in an alkaline solution and then by conversion of this to allyl ester of acetylthiosulfanilic acid.

SUMMARY

1. By an example taken from synthesis of potassium acetylthiosulfanilate there was confirmed the mechanism of the reaction of preparation of salts of thiosulfonic acids from halides of sulfonic acids and hydrosulfides of alkali metals through the intermediate stage of formation of salts of sulfinic acids.

2. It was shown that it is possible to synthesize the thiosulfonates from salts of sulfinic acids and elemental sulfur.

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A STUDY OF THE MECHANISM OF DIAZOEXCHANGE* IN AZO DYES OF THE NAPHTHALENE SERIES MADE BY MEANS OF THE HEAVY NITROGEN ISOTOPE

B. A. Geller

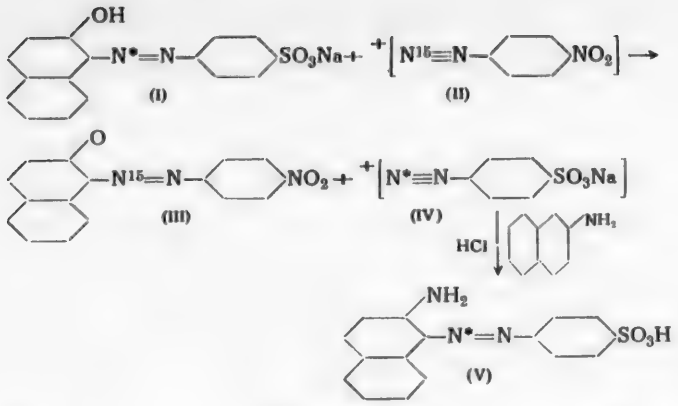
A transfer of a diazo group is a phenomenon which is rather often met in the chemistry of dyes. To this group of reactions belong, for example, the transformation of the mixture of p-sulfobenzenediazonium chloride with p-toluidine into sulfanilic acid and p-toluenediazonium chloride, discovered by Gries [1], the preparation of mixed aminoazo compounds from primary aromatic amines and diazo compounds in weakly acid media [2] and others. Saunders connects these phenomena with the existence in the solution of an equilibrium between the diazo compound, the salt of the amine and nitrous acid formed in hydrolysis.

Replacement of diazo compounds by other diazo compounds was found also in the series of stable azo compounds. Thus, L'vov [3], evidently was the first to discover that in the action of p-nitro- or o-chloro-p-nitrobenzenediazonium compounds on p-sulfobenzeneazo-β-naphthol in an alkaline medium there are formed respectively p-nitro- or o-chloro-p-nitrobenzeneazo-β-naphthols. Analogous reactions were studied more extensively by Filippychev and Chekalin [4]. According to their data, the diazo compounds containing the more negative substituents and behaving more actively in the usual azo coupling, displace the less active diazo compounds from dyes. In the series of substances studied by these authors the following disposition was found in order of activity of the diazo compounds: p-nitroaniline > benzidine > dianisidine > sulfanilic acid > amino-C-acid > α-naphthylamine > m-xylidine > aniline > p-aminosalicylic acid, in which series each compound displaces the following ones from dyes. It was also established that the diazo exchange does not occur with azo components from the benzene series. Using the analogy with other reactions in the naphthalene series [6, 9], the authors suggest that diazoexchange should proceed through the formation of an unstable intermediate with quinoid structure.

In this work there was studied, for the clarification of the mechanism of diazoexchange and specifically the location of the bond rupture, the reaction of 4-sulfobenzene-1-azo-2-naphthol (acid orange) (I) with p-nitrobenzenediazonium hydroxide (II)** using the heavy nitrogen isotope. In one series of experiments the reaction was run with (II) prepared from p-nitroaniline and labeled sodium nitrite with 9.0% of N^{15}. In this case the labeled nitrogen atoms are shown in reaction scheme (1) below by the symbol N^{15}. The other nitrogen atoms must be regarded as unenriched ones (i.e., with 0.37% of N^{15}) regardless of the symbols used. In another series of experiments the heavy nitrogen was introduced into (I) by coupling sulfanilic acid diazotized with $NaN^{15}O_2$ with β-naphthol. In this case the nitrogen atoms with 9% of N^{15} and shown as N^* while the other nitrogen atoms (regardless of symbols) are plain atoms with 0.37% of N^{15}. The study was made by the scheme:

*The term "diazoexchange" used not too satisfactorily at times in the transfer of one diazo group in coupling reactions of diazo compounds with primary aromatic amines in weakly acid media, reflects well the nature of reactions similar to that studied in this work. Since diazo groups cannot move of themselves, it is clear that the term diazoexchange means an exchange in which diazo compounds participate (diazo components).

**The hydrochloride of (II), used for the reaction, is transformed into the diazonium hydroxide under the conditions of alkaline medium which results from mixing of the solutions.



(1)

After the diazoexchange, the separated p-sulfobenzenediazonium compound (IV) was coupled with β-naphthylamine. The dyes (III) (para red) and (V) were purified, the nitrogen contained in them was converted to ammonium chloride and this was subjected to isotope analysis. The results of the analyses are given in Table 1. The analysis of the dyes in the first series of experiments showed that practically all the excess of N^{15} (over the natural content of 0.37% of N^{15}) is located in (III). The results of the second series of experiments showed that the N^*-atom in (I) does not enter the dye (III), i.e., that the link of this nitrogen atom to the naphthalene nucleus is ruptured.

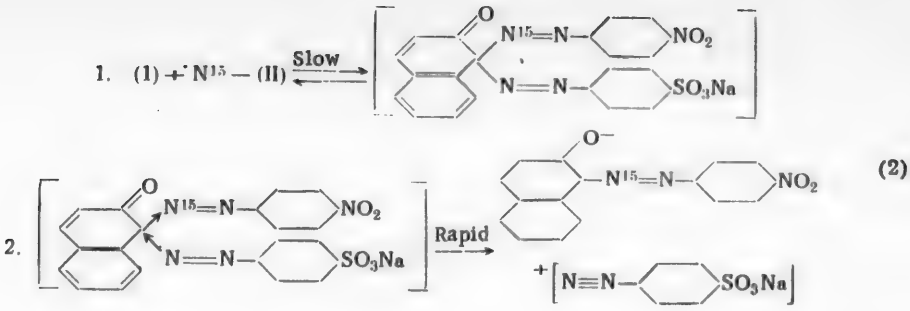
Therefore, the diazo components preserve during the transfer the nitrogen atoms belonging to them. The distribution of N^{15} which corresponds to this is shown in scheme (1). This result agrees with the mechanism of an electrophilic displacement, commonly accepted at present for the reaction of azo coupling. Evidently, the diazoexchange should be regarded as an example of azo coupling in which the site of attack by the diazonium ion occupied not by hydrogen but by some other substitutent. Many cases are described in the literature for diazo coupling with a simultaneous displacement of SO_3H, COOH, Br, I, CHO, and other groups [5-8]. In the present

TABLE 1

Reaction products	Starting substances: 1st series (I) – unlabeled 0.37% N^{15}			Starting substances: 2nd series (II) – unlabeled 0.37% N^{15}		
	N^{15} (in atom %)					
	found	Calculated for: scheme (2)	Calculated for: scheme (3)	found	Calculated for: scheme (2)	Calculated for: scheme (3)
Dye (III)	3.1 2.8	3.25	0.37	0.42 0.51	0.37	3.25
Dye (V)	0.63 0.71	0.37	3.25	—		

*Numbers under nitrogen atoms indicate the content of N^{15} in them.

case the displaced substituent is another diazo compound. The analogy with azo coupling may be seen also in the coincidence of the series of diazo compounds which displace each other, shown above, with the series made in order of their activities. Thus the reaction of the diazoexchange should proceed through an intermediate complex of quinoid type [5, 10, 11] which may be represented by scheme (2).

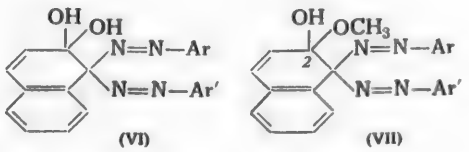


(2)

Since the hydroxy compounds of naphthalene participate in the azo coupling reaction in the form of naphtholate ions, in scheme (2) we mean the ion $-OC_{10}H_6N_2C_6H_4SO_3Na$ to be the substance (I).

Our results, obtained with N^{15}, do not permit us to make a selection between mechanisms S_E2 and S_E3. However, as it was shown by the study of the kinetic isotope effect of hydrogen [10], azo coupling in all cases proceeds in two stages by S_E2 mechanism. There is no basis to consider that the diazoexchange proceeds differently from azo coupling in which the formation of the intermediate complex is complicated by steric hindrance. Therefore one may assume that diazoexchange also proceess by the S_E2 mechanism.

The intermediate complex of quinoid type (VI), proposed by Filippychev and Chekalin [4], cannot form in diazoexchange in hydroxy azo dyes, since hydroxy compounds enter this reaction, as well as that of diazo coupling, in the form of phenolate (or naphtholate) ions. Therefore there is no basis to bring OH groups at this point of discussion. The electron density at the ion $-O-C$ is sufficient to compensate for the positive charge of carbon. It is possible, however, that in the diazoexchange of ethers of naphthols, in which the alkyl groups are not cleaved, there occurs the formation of an intermediate complex (VII) since in this case the electrons of oxygen of the methoxy group cannot completely compensate for the positive charge on carbon C_2 caused by the attack of the electrophilic reagent.



(VI) (VII) (3)

Diazoexchange may differ in the details of the mechanism of electrophilic displacement from the usual azo coupling in which a displacement of a proton occurs. The cleavage of the proton from the transitional complex may be aided by the acceptors HO^-, H_2O and others, which are present in the reaction medium, since hydrogen by the steric conditions is readily available to the ions or molecules surrounding it and, in addition, is susceptible to formation of hydrogen bonds. Conversely, nitrogen in a complex molecule of the azo compound does not possess such properties and therefore it must be supposed that the donor-acceptor mechanism plays but a small role in the cleavage of the diazonium cation in the diazoexchange.

It is also impossible to accept that the displacement of diazo compounds is determined by the relative stabilities of the reacting diazonium cations, since it is specifically the more stable cation that enters the compound while the less stable one is liberated and passes into solution.

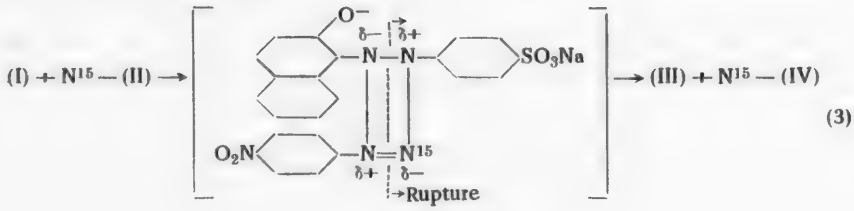
It is most probable that the decomposition of the transitional complex is aided by an electron shift in the system of the joined diazo compounds [as shown in scheme (2)] directed toward the more electrophilic diazo compound.

The reaction of diazoexchange, as indicated above, does not occur in dyes with azo components of the benzene series. This may be explained only by the lesser tendency of the benzene derivatives to form quinoidal structures. The ability of various systems to form quinones is characterized by their oxidation potential. With

introduction of electron-donor substituents (in case of naphthalene – a second benzene ring) which increases the total electron density, the oxidation potential of quinones decreases. Thereby both the formation of quinones and the progress of reactions of electrophilic displacement are facilitated.

The reactions of usual coupling proceed both in benzene and naphthalene series. The absence of a sharp distinction in these cases is connected with the fact that hydrogen, unlike the arylazo group, does not lower the negative charge of the carbon which is being attacked. However, as shown by Burmistrov [5], the smaller oxidation potential of quinones is displayed here as well in the form of greater rate of azo coupling.

The results obtained in this work permit us to refuse the mechanism which might be suggested on the basis of a number of analogies and abilities of nitrogen atoms to form chains and rings.* The distribution of N^{15} in this case is opposite to what was found experimentally (Table 1).



(3)

EXPERIMENTAL

Sodium nitrite $NaN^{15}O_2$ was prepared from ammonia with 9.0% of N^{15} by the scheme:

$$N^{15}H_3 \xrightarrow[Pt,\ 600°]{O_2} N^{15}O_2 \xrightarrow{Ba(OH)_2} Ba(N^{15}O_3)_2 + Ba(N^{15}O_2)_2 \xrightarrow{H_2O_2}$$
$$\rightarrow Ba(N^{15}O_3)_2 \xrightarrow{Na_2SO_4} NaN^{15}O_3 \xrightarrow[350°]{Pb} NaN^{15}O_2$$

Oxidation of ammonia with air over platinum catalyst was run in a flow system at 600°, the velocity of the gas stream being 10 liters per hour with the content of ammonia being 8% or lower. Evidently, owing to the unstable conditions, it was impossible to attain high yields of NO_2: these reached 60-65%. The nitrogen oxides were absorbed by a saturated solution of barium hydroxide and were finally frozen out with liquid air. Solid nitrogen dioxide was then treated with the same barium hydroxide solution in hermetically tight apparatus. Excess barium hydroxide was removed by passage of carbon dioxide stream into the solution. The barium carbonate was filtered off after boiling and the solution, now acidified by 2-3 drops of concentrated nitric acid, was oxidized with hydrogen peroxide with heating to 70°. The solution was neutralized with barium hydroxide (its excess was again removed with carbon dioxide) and was evaporated to dryness after filtration. The resulting $Ba(N^{15}O_3)_2$ was transformed into $NaN^{15}O_2$ by treatment with an equivalent amount of sodium sulfate in a hot solution.

By heating $NaN^{15}O_2$ with lead powder to 350°, the former was changed into $NaN^{15}O_2$ [14, 15].

N^{15}-Acid orange (I) labeled with heavy nitrogen was prepared by diazotization of sulfanilic acid with sodium nitrite containing 9.0% of N^{15} with subsequent coupling with β-naphthol. The dye was recrystallized three times from water for removal of sodium chloride.

Diazoexchange between Acid orange and p-nitrobenzenediazonium compound. The conditions for the diazoexchange were so selected as to secure a good yield of (III) at the same time producing the optimum conditions for coupling of (IV) with β-naphthylamine. One g (0.0028 mole) of (I) was dissolved in water with 0.8 g of sodium carbonate and was then mixed with p-nitrobenzenediazonium chloride, prepared from 0.26 g of p-nitroaniline (0.0019 mole) with 0.9 ml of concentrated hydrochloric acid, at 0°. The medium remains alkaline during this

*Formation of intermediate cyclopentazanes was proposed for the reaction of diazo compounds with hydrazoic acid and has been confirmed by isotope studies [12]. Formation of mixed four-membered rings from nitrogen and carbon atoms may occur in the presence of azo- or methylenimino group [13]; here the cyclodimers decompose instantly at times, while at times they are obtained in the form of stable compounds.

operation. After 30 minutes standing in ice the precipitate of (III) and (I) was filtered off as rapidly as possible. The filtrate was acidified with 7 ml of concentrated hydrochloric acid and mixed with the hydrochloric acid solution of 0.27 g of β-naphthylamine. The precipitated dyes were filtered off after several hours, washed with water and dried. The p-nitrobenzeneazo-β-naphthylamine was extracted with hot benzene and the residual (V) was recrystallized from alcohol (3 : 1).

The precipitate of (III) and (I) was washed on the filter with hot water until the filtrate became only slightly pigmented. The (III) which remained on the filter was dried and repeatedly recrystallized from glacial acetic acid. The yields of crude dyes were 50-60% of theoretical.

Qualitative analysis (fusion with metallic sodium) failed to show any sulfur in (III); the tests of an aqueous extract with p-aminodiethylaniline, sodium nitroprusside and lead acetate were all negative. This shows the absence of admixtures of (I) and (III). In connection with this fact we are unable to explain the deviations in the content of N^{15} in (III) from values computed by scheme (2). The cause for this may lie in the parallel progress of the process by mechanism (3); however the degree of its participation may make up 2-5% which lies close to the experimental error.

TABLE 2

Number of recrystallizations	% N^{15} in (III)
2	0.59
3	0.44
4	0.52
5	0.47
6	0.53
Average	0.51

The control of purity of dye (III) in one experiment was also made by the determination of the isotopic composition of nitrogen after each crystallization. As it is evident from Table 2, the isotopic composition is practically unchanged after the third recrystallization.

The small variations may be explained by the difficulty of the treatment of N=N and NO_2 groups by the Kjeldahl method: there occurs the elimination of heavy or light nitrogen, respectively, in insignificant volumes which cannot be subjected to any computation.

The dyes were qualitatively identified by their physical properties (color, solubility) with those prepared synthetically from individual substances. In addition, the melting point of (III) was determined; this agreed with the literature data.

Isotopic Nitrogen Analysis

A portion of the dyes was treated by the Kjeldahl method altered for nitro and azo compounds [16]. The method was checked with dye (III) that was synthesized by us and gave satisfactory results. The ammonia was distilled from reaction mixture into hydrochloric acid. The resulting ammonium chloride was precipitated with sodium cobaltinitrite * from aqueous alcoholic solution (1 : 1) and was again converted to ammonia by decomposition of the precipitate with alkali.

The isotopic analysis of nitrogen samples, obtained from the ammonium chloride by hypobromite oxidation, was run in a mass spectrometer by the measurement of 28 and 29 peaks. The relative errors of the determination were not over 2-3%. The results are shown in Table 1.

I thank A. I. Brodskii for his aid in this work.

SUMMARY

The diazoexchange in azo dyes of the naphthalene series was studied on the example of reaction between p-sulfobenzeneazo-β-naphthol and p-nitrobenzenediazonium hydroxide. The results, obtained with the aid of labeled nitrogen, agree with the mechanism of an electrophilic displacement. Suppositions were made about the details of the mechanism of the reaction of diazoexchange.

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* The reagent for precipitation was prepared by solution of 11.25 g of $Na_3Co(NO_2)_6 \cdot 0.5\ H_2O$ and 12.50 g of $NaNO_2$ in 100 ml of water. The solution was filtered after one day.

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*Original Russian pagination. See C. B. Translation.
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REACTION OF N,N-DICHLOROBENZENE SULFONAMIDE WITH POLYHALOGEN DERIVATIVES OF METHANE. I.

A. E. Kretov and M. M. Kremlev

An evolution of chlorine and formation of benzenesulfonyl chloride was observed by us on heating N,N-dichlorobenzenesulfonamide (Dichloramide B) with carbon tetrachloride in the presence of anhydrous aluminum chloride. The chlorine evolution was so abundant that it demanded the supposition that carbon tetrachloride took part in the reaction (the carbon tetrachloride was used in a large excess).

Experiments with various amounts of the dichloramine and aluminum chloride gave the following results (Table 1).

TABLE 1

Taken for the reaction (in moles)			Obtained (in moles)	
Dichloramine B	$AlCl_3$	CCl_4	Cl_2	$C_6H_5SO_2Cl$
0.1	0.1	1.55	0.202	0.050
0.1	0.2	1.55	0.204	—
0.2	0.1	1.55	0.198	0.104
0.3	0.1	1.55	0.226	—
0.4	0.1	0.62	0.340	—

In the reaction of three and four moles of dichloramine B with one mole of aluminum chloride in carbon tetrachloride, there remained some unreacted dichloramine B after even thirty hours of heating. It was decided, therefore, in the study of this reaction to limit ourselves to two ratios of dichloramine B to aluminum chloride; specifically 2:1 and 1:1.

One of us has shown previously that anhydrous aluminum chloride reacts energetically with dichloramine B in the ratio of 1:1 in the medium of aromatic hydrocarbons, with formation of the corresponding oily complex and an equimolar amount of the chlorinated hydrocarbon.

Evidently, in case of carbon tetrachloride there is formed in the first stage of the reaction an unstable complex with the composition $C_6H_5SO_2\overset{+}{N}Cl\ \overline{A}lCl_4$ and, hence, for the normal course of the reaction it is necessary to take one mole of aluminum chloride per mole of dichloramine B.

With equimolar amounts of dichloramine B and aluminum chloride in an excess of carbon tetrachloride, all the dichloramine B and the aluminum chloride dissolved after but 30 minutes of heating to 34-35°. A heavy viscous light yellow oil collects on the bottom of the flask; this oil decomposes on further heating and evolves chlorine. This decomposition occurs particularly energetically at 50-52°.

Cyanuric chloride is formed in the reaction in addition to chlorine and benzenesulfonyl chloride. The quantitative isolation of these products permits the following summary equation to describe the reaction:

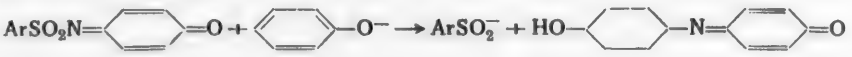
$$3C_6H_5SO_2NCl_2 + 3CCl_4 \rightarrow 3C_6H_5SO_2Cl + 6Cl_2 + C_3N_3Cl_3$$

The reaction is accompanied by the rupture of the bond between the atoms of nitrogen and sulfur.

Not a few such reactions are known among arylsulfonamides and their derivatives. For example, benzenesulfonodialkylamides yield about 70% of benzenesulfonyl chloride and dialkylsulfamic acid [1] on being heated with chlorosulfonic acid.

$$C_6H_5SO_2NR_2 + ClSO_3H \longrightarrow C_6H_5SO_2Cl + R_2NSO_3H$$

It was established, by the studies made by S. N. Burmistrov and E. A. Titov [2] on the indophenol reaction of N-arylsulfonylquinonimines synthesized by them, that these compounds react, in an alkaline medium, with phenol with cleavage of the arylsulfonyl residue in the form of the anion of arylsulfinic acid.



Braun and Rudolph [3] showed that the decomposition of imido chlorides of the structure:

$$C_6H_5SO_2N=C(Cl)-R$$

is accompanied by the formation of benzenesulfonyl chloride and the corresponding nitrile. There are also known many examples of hydrolysis of sulfamide derivatives as the result of their being heated with acids [4], especially in the presence of phenols [5], which reactions lead to the formation of amines [6].

The course of the new reaction may be explained by considering the reaction of aluminum chloride with dichloramine B which is accompanied by evolution of chlorine.

$$ArSO_2NCl_2 + AlCl_3 \longrightarrow ArSO_2\overset{+}{N}Cl\overset{-}{A}lCl_4,$$
$$ArSO_2\overset{+}{N}Cl\overset{-}{A}lCl_4 \longrightarrow ArSO_2NClAlC_2 + Cl_2.$$

The resulting aluminum compound derivative of dichloramine B reacts further with carbon tetrachloride:

$$ArSO_2NClAlCl_2 + CCl_4 \longrightarrow ArSO_2NClCCl_3 + AlCl_3,$$
$$ArSO_2NClCCl_3 \longrightarrow ArSO_2N=CCl_2 + Cl_2,$$
$$3ArSO_2N=CCl_2 \longrightarrow 3ArSO_2Cl + C_3N_3Cl_3$$

The fact that dichloramine B reacts very readily with anhydrous aluminum chloride speaks in favor of this reaction scheme as does the evolution of chlorine which is observed in simple trituration of these substances in a mortar at room temperature.

In order to check this reaction mechanism there was run an experiment with heating of an equimolar mixture of dichloramine B with anhydrous aluminum chloride on a water bath. In this instance 0.7 mole of chlorine was evolved. No evolution of chlorine was observed during the further heating of the resulting product with carbon tetrachloride.

It appeared that this experiment neglects the above-shown reaction scheme. However, it is impossible to reject this scheme categorically since during the heating of dichloramine B with aluminum chloride in the presence of carbon tetrachloride the resulting aluminum derivative reacts, evidently, instantaneously, with the carbon tetrachloride.

Possibly in the presence of anhydrous aluminum chloride the dichloramine B reacts with carbon tetrachloride by means of free radicals with cleavage of chlorine:

$$CCl_4 \longrightarrow CCl_3\cdot + Cl\cdot,$$
$$C_6H_5SO_2NCl_2 + CCl_3\cdot \longrightarrow C_6H_5SO_2NClCCl_3 + Cl\cdot,$$
$$CCl_4 + Cl\cdot \longrightarrow CCl_3\cdot + Cl_2,$$

$$C_6H_5SO_2NCl_2 + CCl_3^{\cdot} \longrightarrow C_6H_5SO_2NClCCl_3 + Cl^{\cdot} \text{ etc.}$$
$$C_6H_5SO_2NClCCl_3 \longrightarrow C_6H_5SO_2N{=}CCl_2 + Cl_2,$$
$$3C_6H_5SO_2N{=}CCl_2 \longrightarrow 3C_6H_5SO_2Cl + C_3N_3Cl_3.$$

It should be indicated that benzenesulfonamide does not react with carbon tetrachloride under these conditions and that no evolution of chlorine occurs. A complex with the composition $C_6H_5SO_2NH_2 \cdot AlCl_3$ is obtained after the removal of carbon tetrachloride.

Benzenesulfonamide is always detected among the reaction products of N,N-dichlorobenzenesulfonamide with carbon tetrachloride in the presence of anhydrous aluminum chloride, besides the products mentioned above. The presence of this substance among the reaction products may be explained first by the presence of this material in the starting dichloramine and secondly by its formation from dichloramine B through a side reaction:

$$C_6H_5SO_2NCl_2 + 2HCl \longrightarrow C_6H_5SO_2NH_2 + 2Cl_2.$$

The hydrogen chloride is always contained in anhydrous aluminum chloride as indicated by Thomas [7].

EXPERIMENTAL

Into a flask with 500 ml capacity there was placed 150 ml of dry carbon tetrachloride, 26.6 g of aluminum chloride and 45.2 g of dichloramine B and the flask was provided with a reflux condenser. A homogeneous solution formed rapidly after the mixture had been stirred. The flask contents were slowly heated on a water bath with a simultaneous passage of dry air through the system for the displacement of the evolving chlorine. Chlorine was absorbed by 10% solution of sodium hydroxide. An energetic reaction occurred at 50-52° with violent evolution of chlorine. The temperature was raised gradually and the mixture was kept at reflux until the reaction was completed. The duration of the reaction was 4-5 hours. After completion of the reaction, carbon tetrachloride was decanted and the yellow oil which remained in the flask was washed with three portions (100 ml each) of carbon tetrachloride. The combined carbon tetrachloride solution was treated with ice water for the removal of aluminum chloride, was then filtered, dried with calcium chloride and freed of excess carbon tetrachloride by distillation. The residue was distilled in vacuum; benzenesulfonyl chloride distilled with cyanuric chloride in the range of 140-146° (at 25 mm). After their separation by filtration and extraction of cyanuric chloride from the condenser, there was obtained 14.2 g (40%) of benzenesulfonyl chloride and 2.7 g (22%) of cyanuric chloride with m.p. 144-145°.

Found %: Cl 57.20; N 22.44. M 183.4. $C_3N_3Cl_3$. Calculated %: Cl 57.67; N 22.79. M 184.4

Identification of benzenesulfonyl chloride was done by its conversion into benzenesulfonamide. The residue in the flask after the extraction with carbon tetrachloride was treated with ice water with acidification with hydrochloric acid for the removal of aluminum chloride. After drying and recrystallization from ethyl alcohol there was isolated 6.4 g (20%) of benzenesulfonamide; m.p. 152°. No depression was observed in the mixed melting point with pure benzenesulfonamide. The determination of the amount of chloride which had evolved during the reaction was made iodometrically and by the weight increment of the absorption flasks; both methods gave concordant results: 28.2 g (97.5%).

Experiments with doubled amount of dichloramine B in respect to aluminum chloride were run analogously. The duration of the reaction was 12-15 hours. The results of the experiments were approximately the same as with the equimolar ratio of dichloramine B and aluminum chloride, except for the fact that we failed to isolate any benzenesulfonamide in the pure state. There was isolated a product having double the molecular weight of benzenesulfonamide and the corresponding elemental composition. The results of the experiments are shown in Table 2.

We could not isolate cyanuric chloride in large amounts and its yield did not rise over 22-24%. The extraordinary volatility of cyanuric chloride and the losses associated with it constitute the cause of this result. It is sufficient to say that we found pure cyanuric chloride in the distilled benzenesulfonyl chloride as well as in crystalline state even in the tube used for chlorine take-off, despite the presence of a reflux condenser.

The low yield of benzenesulfonyl chloride may be explained by the fact that it forms a complex with aluminum chloride, which hydrolyzes forming benzenesulfonic acid during treatment with water.

$$C_6H_5SO_2Cl + AlCl_3 \longrightarrow C_6H_5\overset{+}{S}O_2\overset{-}{A}lCl_4$$

$$C_6H_5\overset{+}{S}O_2\overset{-}{A}lCl_4 + H_2O \longrightarrow C_6H_5SO_2OH + AlCl_3 + HCl$$

TABLE 2

Starting materials		Products obtained	
formula	amount (in g)	formula	yield (in %)
$C_6H_5SO_2NCl_2$	45.2	Cl_2	95
$AlCl_3$	13.3	$C_6H_5SO_2Cl$	50
CCl_4	240	$C_3N_3Cl_3$	24
		$C_6H_5SO_2NH_2$	30

SUMMARY

N,N-Dichlorobenzenesulfonamide reacts in carbon tetrachloride in the presence of anhydrous aluminum chloride, with formation of benzenesulfonyl chloride, cyanuric chloride and with evolution of chlorine according to the reaction schemes shown above. The reaction proceeds with the greatest rate with equimolar ratio of N,N-dichlorobenzenesulfonamide and aluminum chloride. Benzenesulfonamide always forms from side reactions and its yield rises with the use of a doubled amount of N,N-dichlorobenzenesulfonamide.

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REACTION OF N,N-DICHLOROBENZENESULFONAMIDE WITH POLYHALOGEN DERIVATIVES OF METHANE. II.

A. E. Kretov and M. M. Kremlev

In our first paper we described the reaction of N,N-dichlorobenzenesulfonamide with carbon tetrachloride in the presence of anhydrous aluminum chloride [1].

N,N-Dichlorobenzenesulfonamide should react under analogous conditions with other polyhalogen derivatives of methane. In order to study this reaction, we set up some experiments with chloropicrin and chloroform.

Chloropicrin, which was both a reagent and the medium, was used in large excess in these experiments, while N,N-dichlorobenzenesulfonamide and aluminum chloride were taken in equimolar amounts. It turned out that heat evolution took place on mixing the reactants and an abundant evolution of chlorine occurred along with that of cyanuric chloride even under cooling to 5°.

It was proven by specially set-up experiments that no decomposition of chloropicrin, according to the equation $CCl_3NO_2 \rightarrow COCl_2 + NOCl$ takes place under these conditions under the influence of aluminum chloride.

It appeared that the evolution of nitrosyl chloride and phosgene occurs only on heating of chloropicrin with aluminum chloride almost to boiling.

After introduction of chloropicrin into the flask and cooling to 5°, there was added the aluminum chloride. No evolution of chlorine was observed. After the dissolution of aluminum chloride, the introduction of dichloramine B at 5° resulted in immediate evolution of chlorine and $ClNO_2$. After approximately three hours at 5° all the dichloramine had gone into solution. Bubbles of gases were continually formed in the flask in great abundance.

With gradual elevation of bath temperature to 30° the gas evolution became so abundant that foam appeared on the top of the mixture. A heavy yellow oil collected on the bottom of the flask. Under the conditions of the experiment the nitro group is cleaved from the molecule of chloropicrin and by joining an atom of chlorine forms a molecule of $ClNO_2$ which evolves along with chlorine. The $ClNO_2$ was isolated by us by its condensation in the liquid state.

Analysis of the alkali, through which the gaseous reaction products were passed for quantitative absorption, indicated the presence of the anion NO_3^-. Its presence was proved by six known qualitative tests, among them the microcrystalline reaction with "Nitron." The presence of NO_3^- anion in the alkali may be connected only with the reaction:

$$NaOH + ClNO_2 \rightarrow NaNO_3 + HCl.$$

Consequently the isolation of $ClNO_2$ from the reaction of chloropicrin with dichloramine B cannot be doubted.

The separation and isolation of the reaction products gave a considerable amount of benzenesulfonyl chloride and a smaller amount of cyanuric chloride.

The found amounts of chlorine and $ClNO_2$ correspond to the following summary reaction equation:

$$3C_6H_5SO_2NCl_2 + 3CCl_3NO_2 \rightarrow 3C_6H_5SO_2Cl + C_3N_3Cl_3 + 3Cl_2 + 3ClNO_2.$$

It is possible that the process proceeds in several directions, since benzenesulfonyl chloride and cyanuric chloride were found in smaller amounts.

The reaction mechanism can be explained in this case quite easily by the formation of free radicals in the presence of aluminum chloride:

$$CCl_3NO_2 \longrightarrow CCl_3\cdot + NO_2\cdot$$
$$C_6H_5SO_2NCl_2 + CCl_3\cdot \longrightarrow C_6H_5SO_2NClCCl_3 + Cl\cdot$$
$$CCl_3NO_2 + Cl\cdot \longrightarrow CCl_3\cdot + ClNO_2$$
$$C_6H_5SO_2NCl_2 + CCl_3\cdot \longrightarrow C_6H_5SO_2NClCCl_3 + Cl\cdot \text{ etc.}$$

The resulting N-trichloromethyl derivative of dichloramine is unstable and decomposes with evolution of chlorine as in experiments with carbon tetrachloride [1].

$$C_6H_5SO_2NClCCl_3 \longrightarrow C_6H_5SO_2N{=}CCl_2 + Cl_2$$
$$3C_6H_5SO_2N{=}CCl_2 \longrightarrow 3C_6H_5SO_2Cl + C_3N_3Cl_3$$

Analogous experiments were run in chloroform medium.

It appeared that chloroform also reacts readily with dichloramine B with evolution of chlorine and a small amount of hydrogen chloride.

Among the reaction products there were found by us: benzenesulfonamide, benzenesulfonyl chloride and cyanuric chloride. The formation of chlorine, hydrogen chloride, benzenesulfonyl chloride and cyanuric chloride may be represented by the following equation:

$$3C_6H_5SO_2NCl_2 + 3CHCl_3 \longrightarrow 3C_6H_5SO_2Cl + C_3N_3Cl_3 + 3Cl_2 + 3HCl \quad (I)$$

The formation of a considerable amount of benzenesulfonamide may be explained by the well-known reaction [2]:

$$C_6H_5SO_2NCl_2 + 2HCl \longrightarrow C_6H_5SO_2NH_2 + 2Cl_2 \quad (II)$$

The other schemes for the formation of benzenesulfonamide:

$$C_6H_5SO_2NCl_2 + 2CHCl_3 \longrightarrow C_6H_5SO_2NH_2 + C_2Cl_6 + Cl_2 \text{ and}$$
$$C_6H_5SO_2NCl_2 + 2CHCl_3 \longrightarrow C_6H_5SO_2NH_2 + 2CCl_4$$

can be excluded since no hexachloroethane or carbon tetrachloride were found among the reaction products.

From Equations (I) and (II) we obtain the summary equation for the reaction between chloroform and dichloramine B in the presence of aluminum chloride:

$$9C_6H_5SO_2NCl_2 + 6CHCl_3 \longrightarrow 6C_6H_5SO_2Cl + 3C_6H_5SO_2NH_2 + 2C_3N_3Cl_3 + 12Cl_2 \quad (III)$$

The reaction mechanism remains the same, evidently, as in the case of chloropicrin.

EXPERIMENTAL

Reaction with chloropicrin. Into a flask, with 500 ml capacity, provided with a reflux condenser there was placed 107 g of dried and distilled chloropicrin. With constant cooling to 5° there was added 26.6 g of anhydrous aluminum chloride and 45.2 g of dichloramine B. The evolving chlorine and $ClNO_2$ were displaced from the flask by passage of dry air and were absorbed by 10% solution of alkali. After the dissolution of dichloramine B, the bath temperature was gradually raised from 0° to 30° and was kept at this level for eleven hours. The reaction was completed at bath temperature of 50° after cessation of chlorine evolution. The duration of the reaction was approximately 15 hours.

The weight gain in the absorption flasks was 27.57 g; the amount of chlorine found iodometrically was 14.12 g, and that of $ClNO_2$ found by difference was 13.45 g.

The excess chloropicrin was distilled in vacuum at bath temperature of 50°. The residue in the flask, which was a yellow oil, was subjected to a triple extraction with benzene (100 ml each) at 50°.

Benzenesulfonyl chloride, along with cyanuric chloride, was distilled at 16-18 mm in the range of 132-136°. After filtration from cyanuric chloride there was obtained 24.5 g of benzenesulfonyl chloride.

The residue in the flask, after extraction with benzene, was a dark substance which was then treated with ice water, filtered and dried. An additional amount of cyanuric chloride was removed from it by extraction with ether. In all 2.49 g of cyanuric chloride was isolated. The results of the experiments are shown in Table 1.

TABLE 1

Starting and final products	Taken (in g)	Obtained (in g)	Obtained yield (in %)
$C_6H_5SO_2NCl_2$	45.2	—	—
$AlCl_3$	26.6	—	—
CCl_3NO_2	107	—	—
$ClNO_2$	—	13.45	85
Cl_2	—	14.12	100
$C_6H_5SO_2Cl$	—	24.5	70
$C_3N_3Cl_3$	—	2.49	33

TABLE 2

Starting and final products	Taken (in g)	Obtained (in g)	Obtained yield (in %)
$C_6H_5SO_2NCl_2$	45.2	—	—
$AlCl_3$	26.6	—	—
$CHCl_3$	223	—	—
$C_6H_5SO_2NH_2$	—	17.6	157
$C_6H_5SO_2Cl$	—	7.07	30
Cl_2	—	20.4	107
HCl	—	0.2	—
$C_3N_3Cl_3$	—	1.38	19

Reaction with chloroform. The technique of the experiments was the same as in the reaction with chloropicrin.

Into the flask there was introduced 150 ml of chloroform, 26.6 g of aluminum chloride and 45.2 g of dichloramine B. After termination of the intensive phase of the reaction at 35°, the reaction was brought to completion, i.e., cessation of chlorine evolution, by being gradually heated to the boiling point of the reaction mixture.

The oil remaining in the flask after the decantation of chloroform was extracted with three portions of chloroform of 100 ml each. After treatment with ice water and drying, there was isolated from it by fractional distillation at 23-24 mm at temperature interval of 140-143° the 7.07 g of benzenesulfonyl chloride and the 1.38 g of cyanuric chloride which were separated by filtration.

The total weight gain of the absorption flasks was 20.6 g; the amount of chlorine found iodometrically was 20.4 g, and that of hydrogen chloride found by difference was 0.2 g. The results of the experiment are shown in Table 2.

The residue in the flask after chloroform extraction was treated with ice water with acidification with hydrochloric acid; then it was filtered and recrystallized from water, yielding 17.6 g of benzenesulfonamide.

The yields of products were calculated according to the reaction Equation (III).

The excess yield of benzenesulfonamide and the decreased yield of benzenesulfonyl chloride and cyanuric chloride are of approximately the same magnitude and are explained by the same causes as in experiments with carbon tetrachloride [1].

SUMMARY

N,N-Dichlorobenzenesulfonamide readily reacts with chloropicrin and chloroform, in the solutions in these substances, in the presence of anhydrous aluminum chloride, the reaction being in accord with the summary equations given above.

The reaction with chloropicrin proceeds readily in the temperature interval of 5-50° and that with chloroform at 35-60° with equimolar amounts of dichloramine B and aluminum chloride.

The mechanism of the reactions, which evidently proceed through free radicals, may be represented by the scheme shown above.

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THERMOCATALYTIC TRANSFORMATIONS OF α-TERPINENE OVER GUMBRIN

V. V. Tishchenko and N. S. Lishenkova

Wallach observed the formation of terpinolene in the reaction of sulfuric acid with dipentene with its transformation, on further heating, into α-terpinene [1]. Later Venable showed that the action of activated floridin on dipentene leads to the same results [2]. Rudakov in repeating Wallach's experiments found that the action of small amounts of clay on dipentene at 160-170° causes the formation of terpinolene initially, and then that of α-terpinene. Among the final reaction products he found: Δ^3-p-menthene, p-cymene and about 72% of polymers [3]. The formation of Δ^3-p-menthene and p-cymene, evidently according to Rudakov, occurs as the result of conjugated hydrogenation of α-terpinene.

It appeared interesting to verify the correctness of this supposition since such an isomerization may have a close connection with the problem of origin and transformation of petroleum.

EXPERIMENTAL

α-Terpinene was prepared by dehydration of terpineol with oxalic acid [4]. Cineol, formed along with α-terpinene in this reaction, was bound into a complex by two treatments with resorcinol, from which complex the α-terpinene was distilled in vacuum (7 mm) through a column with 40 theoretical plates. The isolated product had the following constants: b.p. 173-175° (760 mm), d^{20}_4 0.8410, $n^{20}D$ 1.4769. The nitrosite prepared according to Wallach's directions [5] melted at 155°.

Gumbrin (a clay of montmorillonite type) activated with hydrochloric acid was used as the catalyst for the thermocatalytic transformation of α-terpinene. The experiments were run in a round bottomed flask with a stirrer and a reflux condenser. The flask was immersed in an oil bath heated to 150-170°.

The conditions at which the polymerization of α-terpinene is reduced to a minimum were determined by preliminary experiments. It was shown that the polymerization depends first of all on the amount of the catalyst used in the experiment. The duration and the temperature in the experiment have only a secondary significance.

In the first experiments α-terpinene was heated with 1% of the catalyst at 150° for one hour. These conditions failed to produce any significant changes in the product, which after the experiment distilled within a narrow range, while the index of refraction changed only insignificantly.

The product obtained after the first such heating was again heated with a new portion of the catalyst (1%). However, the second heating did not cause a significant change of composition, as indicated by the distillation and the determination of the index of refraction, and it was impossible to prove the presence of any p-menthene and p-cymene in this material. The subsequent heating with a new portion of the catalyst for two hours gave a different result. The product (95.5 g) separated from the catalyst was separated by three distillations through a column with 20 theoretical plates at 5 mm into nine fractions each of which boiled within a 2° range. Density and index of refraction were determined for each fraction. Most interesting were the first and the ninth fractions whose constants approached closely to those of p-menthene and p-cymene.

1st fraction, b.p. 165-166° (760 mm), d^{20}_4 0.8280, $n^{20}D$ 1.4608.
9th fraction, b.p. 175-177° (760 mm), d^{20}_4 0.8575, $n^{20}D$ 1.4896.

The small volumes of the first (1.56 g) and the ninth (2.22 g) fractions hindered their study. In order to have them in sufficient amounts, the following experiment was set up. Terpinene (124.2 g) was heated for three hours

at 170° with 3% of the catalyst. There was obtained 104.5 g (84.2%) of the catalyzate which was separated by three distillations at 7 mm into five two-degree fractions.

The first fraction (3.50 g) with b.p. 172-173°, d^{20}_4 0.8296 and $n^{20}D$ 1.4610 approached very closely the constants for dihydrophellandrene or Δ^1-p-menthene reported by Semmler [6] (b.p. 171-173°, d^{20} 0.829, n_D 1.4601).

Found %: C 87.20; H 13.15. M 137. $C_{10}H_{18}$. Calculated %: C 86.95; H 13.05. M 138.

Δ^1-p-Menthene was determined in two samples of the first fraction by means of benzoyl hydroperoxide according to Nametkin [7]. Its content was found to be 96.75%.

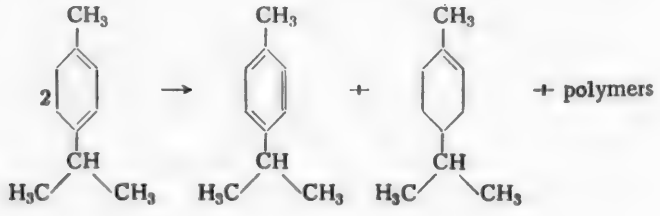
The fifth fraction (19.39 g) boiling at 175-176° (760 mm) and having d^{20}_4 0.8561 and $n^{20}D$ 1.4896, corresponded to p-cymene.

Found %: C 89.65; H 10.25. M 135. $C_{10}H_{14}$. Calculated %: C 89.55; H 10.45. M 134.

Three g of the fifth fraction was oxidized with an alkaline solution of potassium permanganate according to Wiedman [8]. From the products of oxidation there was isolated terephthalic acid, whose basicity number was found to be equal to 1.92 by a titration with 0.1 N alkali. The solution remaining after the isolation of terephthlialic acid was acidified and subjected to extraction with ether. The oil remaining after the distillation of ether solidified on standing into a crystalline mass from which there were isolated, after recrystallization from water, the long needles of p-hydroxyisopropylbenzoic acid, m.p. 155-156°.

The second, third and fourth fractions, boiling respectively at 49-50°, 50-51° and 51-52° (7 mm) and having $n^{20}D$ 1.4788, 1.4818 and 1.4862, were treated with the Beckmann mixture [9] in order to establish the presence of α-terpinene in them. The latter was discovered in noticeable amounts in the second and third fractions, while in the fourth fraction its presence was insignificant. These fractions evidently contain various mixtures of α-terpinene and p-cymene.

The formation of Δ^1-p-menthene and p-cymene in these experiments may be explained by the following scheme:



The resulting polymers with d^{20}_4 0.9358 had the following elemental composition.

Found %: C 88.56, 88.67; H 11.16, 11.27.

The molecular weight determined by the cryoscopic method was equal to 279. These results indicate that the polymers are represented by the diamer of α-terpinene.

SUMMARY

The isomerization of the α-terpinene on gumbrin was studied at 150-170°. It was shown that α-terpinene isomerizes into Δ^1-p-menthene and p-cymene as the result of disproportionation of hydrogen.

The polymers which are formed in the isomerization of α-terpinene consist of the dimer of terpinene.

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THE COMPLEX – PYRIDINE-CUPROUS CHLORIDE – AS AN AUTOXIDATION CATALYST

I. PREPARATION OF AZO COMPOUNDS FROM PRIMARY AROMATIC AMINES

A. P. Terent'ev and Ia. D. Mogilianskii

Azo compounds are often present among the numerous oxidation products of primary aromatic amines. Instances of catalytic effect of some substances on the oxidation of aniline by air have been described as the result of which more or less considerable amounts of azobenzene are formed [1-3]. However, owing to the not very high yields because of a number of side reactions, the reactions of oxidation of arylamines have not received a practical application for the preparation of azo compounds.

It was established by us that oxidation with air or gaseous oxygen of aromatic amines in pyridine solution in the presence of cuprous chloride does lead in a number of cases to smooth formation of azo compounds with a minimum amount of byproducts. Thus, p-azotoluene is obtained thereby in practically quantitative yield while its main bulk crystallizes directly from the reaction mixture owing to its low solubility in pyridine.

Oxidation by this method proceeds very smoothly for benzidine which yields a rather high yield of p,p'-diaminoazobiphenyl. Willstätter and Kalb [4] first prepared this compound in a 15% yield. The substance is isolated directly in a rather pure state in 72% yield by the technique described by us.

In case of other amines (aniline, p-anisidine) there is observed some tar formation, which is rather considerable if the reaction is run with heating. However, the side reactions are severely restricted by passage of pure oxygen at room temperature and by the use of more dilute solutions (about 11 ml of pyridine per 0.1 mole of amine) since in the concentrated solutions there occurs a considerable heat evolution of the mixture which aids tar formation.

The amount of cuprous chloride affects the yield of the azo compound but slightly. Thus, a 77% yield was obtained with the use of 0.8% of cuprous chloride in respect to the amount of the amine.

It was interesting to study the problem of the nature of the catalyst in this reaction and of the mechanism of its action. Insofar as the catalytic effect was discovered in a pyridine solution in the presence of cuprous chloride, it followed naturally that the significance of each of these components should be examined. With the example of p-toluidine we subjected to investigation the possibility of replacement of cuprous chloride by such salts as $FeCl_2$, $FeCl_3$, $CoCl_2$, $CuCl_2$, Cu_2Br_2 and Cu_2I_2. In all these cases the oxidation of amines was not observed at all; however, it began immediately after addition of cuprous chloride.

Also specific is the role of pyridine in this reaction since it cannot be replaced by alcohols, dioxane, dichloroethane or quinoline. In all these cases the oxidation of amines proceeds very slowly, while the amount of consumed oxygen exceeds but slightly the amount needed to oxidize the cuprous ion to cupric. However, after addition of pyridine the oxygen absorption becomes quite energetic.

On the basis of the above data we conclude that the active agent in this reaction of catalytic autoxidation is a complex of pyridine and cuprous chloride since the catalytic influence appears only in the presence of both substances simultaneously.

The effect of complex compounds of a series of metals on autoxidation of polyphenols, aromatic polyamines, thiols and other easily oxidizable compounds in aqueous medium had been studied by K. and Iu. Shibata

[5]. Two compounds $Cu_2Cl_2 \cdot 4Py$ and $Cu_2Cl \cdot 6Py$ were isolated for the first time and described by Lang [6]. The second of these compounds was isolated by us after dissolution of cuprous chloride in pyridine in a sealed ampoule with cooling of the solution. This complex is evidently the catalyst – oxygen carrier in the presently discussed reaction. As it was shown by us, a solution of cuprous chloride in pyridine absorbs 1 gram atom of oxygen per mole of cuprous chloride. The product of oxidation on being mixed with p-toluidine in nitrogen atmosphere gives up all the oxygen for dehydrogenation of the latter substance, being transformed itself into $Cu_2Cl_2 \cdot 6Py$ which fact was confirmed by analysis for chlorine content.

EXPERIMENTAL

Oxidation of p-toluidine. Into a mixture of 12.5 g of p-toluidine (crystallized with 1 molecule of water), 20 ml of pyridine and 1.25 g of cuprous chloride there was passed at room temperature for two hours a stream of oxygen. Energetic gas absorption was observed along with a noticeable heat evolution. The precipitated scaly crystals (9.6 g) of p,p'-azotoluene were filtered off and washed with a small amount of dilute hydrochloric acid. From the mother liquor there was isolated an additional 0.4 g of p,p'-azotoluene (total yield 95%). After one recrystallization from alcohol the m.p. was 144°.

p-Hydrazotoluene. One g of the above prepared azo compound was dissolved in 100 ml of alcohol. After saturation of the solution with ammonia, hydrogen sulfide was passed into it. After some time there began the separation of colorless scaly crystals which became abundant after addition of a small amount of water. There was isolated 0.8 g of p-hydrazotoluene with m.p. 132-133° (from alcohol), which corresponds to the literature data.

The results of our experiments with some other amines are shown in the table.

Expt. No.	Starting amine		Amt. of pyridine (in ml)	Amt. of Cu_2Cl_2 (in g)	Azo compound obtained			
	Name	Amt. (in g)			Name	M. p.	Yield in g	Yield in %
1	Aniline	9.3	20	1.25	Azobenzene	68°	6.5	71.3
2			100	2.5			8	87.9
3	p-Anisidine	12.3	40	1.25	4,4'-Dimethoxy-azobenzene	162	8.5	70
4		2.5	20	0.25			2	50
5	1,3,4-m-xylidine	12	40	1.25	2,4,2',4'-Tetra-methylazobenzene	129	8	66.4
6	Benzidine	20	100	2	4,4'-Diaminoazo-biphenyl	285—286	14.5	72.5

Experiments 2 and 4 were run to clarify the effect of dilution.

The isolation of the azo compound shown in the table (except the last compound, which precipitated directly) was done by us in two ways: a) pyridine was distilled off in vacuum and the residue was extracted with ligroine; andb) after distillation of the major part of pyridine, dilute hydrochloric acid was added to the residue, thus dissolving the copper salts, and the crude product was extracted with ether which left behind a small black precipitate.

Clarification of the Role of the Catalyst

a) Amount of oxygen absorbed by the catalyst. Into a small flask connected by a rubber tube to a gas burette there was placed 10 ml of pyridine and a carefully weighed amount of cuprous chloride. The flask was shaken mechanically until the absorption of oxygen stopped.

0.32, 0.64 g Cu_2Cl_2: 20.0, 40.0 ml O_2 (746 mm, 16°). Calculated: 19.9, 39.8 ml O_2 (calculated on 1 gram atom of oxygen per mole of cuprous chloride).

b) Transfer of oxygen. Cuprous chloride (0.96 g) in 15 ml of pyridine was saturated with oxygen. There was absorbed 60.5 ml (744 mm, 18°). The product of oxidation was transferred into an ampoule. After displacement

of air by nitrogen, there was added 1 g of p-toluidine and the ampoule was sealed. Soon there was observed a change of color to dark orange and the formation of thin needle-like crystals. After two hours the ampoule was opened and to its contents there was added some dilute hydrochloric acid. The resulting orange precipitate was filtered off, washed with dilute hydrochloric acid and dried at 100-120°. There was isolated 0.5 g of p-azotoluene; calculated amount (on basis of oxygen) was 0.51 g of azotoluene.

Another analogous experiment was run for the purpose of isolation and study of the needle-like crystals which appear in the ampoule. The liquid was sucked from them in an atmosphere of hydrogen and the crystals were washed with a small volume of pyridine and were rapidly and thoroughly pressed on filter paper. A sample was transferred into a previously weighed container for determination of chlorine by the gravimetric method.

Found %: Cl 10.76. $Cu_2Cl_2 \cdot 6Py$. Calculated %: Cl 10.54.

SUMMARY

1. Primary aromatic amines are oxidized by molecular oxygen in pyridine solution in the presence of cuprous chloride, forming azo compounds.

2. The catalyst in this reaction is a complex $Cu_2Cl_2 \cdot 6Py$, which adds oxygen readily and gives it up readily for dehydrogenation of the amine. Cuprous chloride cannot be replaced in this reaction by other salts, including copper salts. Replacement of pyridine by other solvents, as for example alcohol, dioxane, toluene, dichloroethane and quinoline, also gives negative results. The process proceeds most smoothly with pure oxygen at room temperature.

3. The present reaction may be used as a convenient method for the preparation of some azo compounds (p-azotoluene, p,p'-diaminoazobiphenyl, p,p'-dimethoxyazobenzene).

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INDOLE DERIVATIVES

V. SYNTHESIS OF BIS-QUATERNARY AMMONIUM SALTS OF HARMINE

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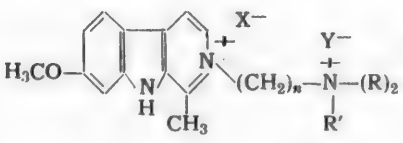
The reports concerning the physiological activity of unsymmetric bis-quaternary ammonium salts, which have appeared recently, [1-3] indicate certain possibilities which are opened by this class of compounds in the search for new gangliolytic and hypotensive preparations.

In this connection we have accomplished the synthesis of some compounds of this class, using as starting material the readily available alkaloid harmine. The compounds prepared by us may present a definite point of interest since, on one hand, it is specifically the bis-quaternary salts of β-carbolines that turned out to be active to the greater degree [1-3], while, on the other hand, harmine itself, as it is known, possesses some hypotensive action.

We prepared compounds of the general type as follows:

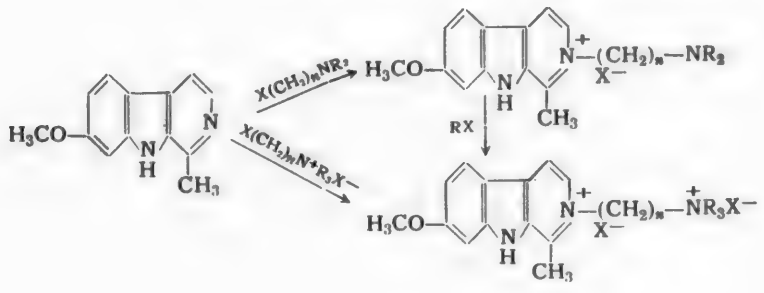


	X	Y	R	R′	n
(I)	I	I	C_2H_5	CH_3	2
(II)	Cl	Br	C_2H_5	C_2H_5	2
(III)	I	I	CH_3	CH_3	2
(IV)	I	I	C_2H_5	C_2H_5	2
(V)	Cl	I	C_2H_5	CH_3	3
(VI)	Cl	Br	C_2H_5	C_2H_5	3
(VII)	Br	Br	C_2H_5	C_2H_5	4

In addition there was prepared, bytthe reaction of harmine with ethylene bromide, the symmetric bis-quaternary salt – the dibromide of 1,2-bis(Py-N-1-methyl-7-methoxy-β-carbolinium)ethane (VIII), as well as the monoquaternary salt of harmine with benzyl chloride – the chloride of Py-N-benzyl-1-methyl-7-methoxy-β-carbolinium (IX).

The preparation of compounds (I)-(VII) was performed in two ways. The first variant of the synthesis consisted of the reaction of harmine with the appropriate dialkylaminoalkyl halide by heating in a mixture of toluene with nitrobenzene with the subsequent reaction of the resulting monoquaternary salt with an alkyl halide.

The second path consisted of the direct reaction of harmine with the corresponding ω-haloalkylammonium salt in boiling butyl alcohol or mixture of toluene with nitrobenzene with the direct formation of the bis-quaternary salt.



The yields of both methods varied within the limits of 54-74%. The bis-quaternary salts with n = 2 were prepared by the first method which turned out to be the more suitable method in this case since it eliminates the preparation of the ω-haloalkyl quaternary salt. However, the use of this method for the synthesis of compounds with n = 3 and n = 4 turned out to be impossible since under the relatively drastic conditions of the condensation, the dialkylaminopropyl halide and, especially, the dialkylaminobutyl halide are quite unstable and suffer an intra- or intermolecular condensation. Owing to this, the compounds with n = 3 and n = 4 were prepared by the second method. The ω-haloalkyl quaternary salts necessary for this were prepared by the recently described convenient method [4] or by the reaction of dialkylaminoalkyl halide with an alkyl halide.

The greatest experimental difficulties in the preparation of the compounds (I)-(VII) were connected with the very low solubility of harmine in the majority of organic solvents. The use of acetonitrile as the solvent, recommended by American authors [2] also failed to give the needed effect (the solubility of harmine even in this case was but 1 g per 250-270 ml of acetonitrile). Therefore, after a long search, we made use of a mixture of nitrobenzene with toluene and, although this combination still had its deficiencies, it did give the best results.

The compounds (I)-(VIII), prepared by us, as well as (VIII) and (IX) were tested at the Pharmacology Department of the Institute by D. A. Kharkevich. The results indicate that compounds (VIII) and (IX) are not interesting, that compounds (I)-(VII) do possess a hypotensive activity which agrees with the data on the bis-quaternary salts of the β-carboline series [3]. The compounds with n = 2 are the more active ones in respect to the depth and the duration of the hypotensive action; lengthening of the aliphatic chain to n = 3 or n = 4 lowers the hypotensive effect to a considerable degree. The greatest interest, among these compounds, is in compound (III) which while having the greatest hypotensive effect is also the least toxic one.

EXPERIMENTAL

Reaction of Harmine with Dialkylaminoalkyl Halides

Chloride of Py-N-(2-diethylaminoethyl)-1-methyl-7-methoxy-β-carbolinium. One g of harmine, 0.66 g of diethylaminoethyl chloride, 4 ml of anhydrous toluene and 4 ml of freshly distilled nitrobenzene were heated at reflux for 20 minutes, cooled, the precipitated crystals being separated, washed several times with small portions of acetone and recrystallized from 80% aqueous dioxane. There was obtained 1 g (62%) of the product with m.p. 204-206°.

Found %: N 11.87, 11.81; Cl 9.99, 9.96. $C_{19}H_{26}ON_3Cl$. Calculated %: N 12.07; Cl 10.19.

Hydrochloride. One g of the above substance was dissolved in anhydrous alcohol and treated with a methanolic solution of hydrogen chloride until a definitely acid reaction was produced. The precipitated crystalline mass was separated, washed with anhydrous alcohol and recrystallized from anhydrous alcohol. The yield was 0.85 g (77.2%); m.p. 257-259°. The literature data [5]: m.p. 252-253°.

Found %: C 59.10, 59.04; H 7.19, 7.24; Cl 18.33, 18.46. $C_{19}H_{27}ON_3Cl_2$. Calculated %: C 59.37; H 7.08; Cl 18.45.

Di-iodide of Py-N-(2-diethylmethylammoniumethyl)-1-methyl-7-methoxy-β-carbolinium (I). One g of the chloride of Py-N-(2-diethylaminoethyl)-1-methyl-7-methoxy-β-carbolinium and 0.96 g of potassium iodide in 60 ml of alcohol was refluxed for 1.5 hours on a water bath, filtered and the filtrate treated with 0.8 g of methyl iodide and the solution refluxed for 1.5 hours longer, cooled and filtered; the crystalline precipitate was washed with a small volume of alcohol and recrystallized from methanol. There was obtained 1 g (62%) of the product with m.p. 228-230°.

Found %: N 7.30, 7.29; I 43.49, 43.69. $C_{20}H_{29}ON_3I_2$. Calculated %: N 7.05; I 43.66.

Chloride bromide of Py-N-(2-triethylammoniumethyl)- 1-methyl-7-methoxy-β-carbolinium (II). One g of the chloride of Py-N-(2-diethylaminoethyl)-1-methyl-7-methoxy-β-carbolinium and 0.33 g of ethyl bromide were refluxed in 60 ml of alcohol on a water bath for three hours, cooled, the separated crystals filtered off, washed with a small volume of acetone and recrystallized from alcohol. There was obtained 0.9 g (69%) of product with m.p. 264-266°.

Found %: Br + Cl 25.02, 25.28. $C_{21}H_{31}ON_3ClBr$. Calculated %: Br + Cl 25.25.

Di-iodide of Py-N-(2-trimethylammoniumethyl)-1-methyl-7-methoxy-β-carbolinium (III). Reaction of 1 g of harmine with 0.5 g of dimethylaminoethyl chloride was run analogously to the synthesis of (I). There was obtained 0.9 g (60%) of the substance with m.p. 160-180° (with decomposition). To this product there was added 1.04 g of potassium iodide and 30 ml of methanol and the mixture was refluxed on a water bath for 40 minutes. The precipitated crystalline mass was separated, the filtrate was treated with 0.62 g of methyl iodide and the mixture heated at reflux on a water bath for one hour. The crystals were separated after cooling and were recrystallized from 85% alcohol. There was obtained 1.4 g (54%) of the substance with m.p. 236-238°.

Found %: I 45.18, 45.02. $C_{18}H_{25}ON_3I_2$. Calculated %: I 45.88.

Di-iodide of Py-N-(2-triethylammoniumethyl)- 1-methyl-7-methoxy-β-carbolinium (IV). From 1 g of the chloride of Py-N-(2-diethylaminoethyl)-1-methyl-7-methoxy-β-carbolinium, 0.96 g of potassium iodide and 1.5 g of ethyl iodide there was prepared the diiodide (IV) analogously to the diiodide (I). The yield was 1 g (64%); m.p. 234-236° (from water).

Found %: I 42.60, 42.33; N 7.00, 7.17. $C_{21}H_{31}ON_3I_2$. Calculated %: I 42.64; N 7.04.

Reaction of Harmine with ω-Haloalkylammonium salts

3-Chloropropyldiethylmethylammonium iodide. To 5 g of 2-diethylaminopropyl chloride [6] there was added dropwise 4.6 g of methyl iodide in 25 ml of absolute ether and the mixture was refluxed for four hours, cooled, the crystalline mass separated, washed with absolute ether and used for the next step without purification.

Found %: I 43.49, 43.79. $C_9H_{19}NClI$. Calculated %: I 43.17.

3-Chloropropyltriethylammonium bromide. Thirty g of 1-chloro-3-bromopropane was heated on a water bath while 14.1 g of triethylamine in 50 ml of anhydrous benzene was added over one hour with stirring. The reaction mixture was stirred for 12 hours longer at room temperature. Benzene was distilled off in vacuum and the residue was dried with phosphorus pentoxide. There was obtained 16 g (54.9%) of hygroscopic substance with m.p. 105-110°.

Found %: Br 30.76, 30.59. $C_9H_{21}NClBr$. Calculated %: Br 30.92.

1,4-Dibromobutane. This was prepared from tetrahydrofuran by the method which was analogous to the known method of preparation of 1,5-dibromopentane [7]. The yield was 52%; b.p. 107-108° (55 mm), $n^{20}D$ 1.5189.

4-Bromobutyltriethylammonium bromide. This was prepared analogously to the 3-chloropropyltriethylammonium bromide from 30 g of 1,4-dibromobutane and 14 g of triethylamine. The yield was 23 g (52.2%); m.p. 110-120°. It was very hygroscopic.

Found %: Br 25.02, 24.98. $C_{10}H_{23}NBr_2$. Calculated %: Br 25.20.

Py-N-(3-methyldiethylammoniumpropyl)-1-methyl-7-methoxy-β-carbolinium chloride iodide (V). One g of harmine and 1.54 g of 3-chloropropylmethyldiethylammonium iodide in 25 ml of butyl alcohol were refluxed for 3 hours. The crystals were separated without cooling, washed with acetone and recrystallized from 80% aqueous acetone. There was obtained 1.1 g (62%) of the substance with m.p. 266-268°.

Found %: N 7.93, 8.14. $C_{21}H_{31}ON_3ClI$. Calculated %: N 8.33.

Py-N-(3-triethylammoniumpropyl)-1-methyl-7-methoxy-β-carbolinium chloride bromine (VI). The reaction of 1 g of harmine and 2.4 g of 3-chloropropyltriethylammonium bromide was run analogously to the preparation of (V). There was obtained 1.4 g (63%) of product with m.p. 268-270° (from 80% aqueous acetone).

Found %: N 8.79, 8.96; Cl + Br 24.32, 24.22. $C_{22}H_{33}ON_3ClBr$. Calculated %: N 8.92; Cl + Br 24.50.

Py-N-(4-triethylammoniumbutyl)-1-methyl-7-methoxy-β-carbolinium dibromide (VII). One g of harmine, 2.98 g of 4-bromobutyl triethylammonium bromide, 6 ml of freshly distilled nitrobenzene and 6 ml of anhydrous toluene were refluxed for 30 minutes. The crystalline mass which separated from the mixture was filtered off and washed several times with acetone. After recrystallization from 80% aqueous acetone there was obtained 1.9 g (77.6%) of product with m.p. 252-254°.

Found %: N 8.01, 8.13; Br 29.69, 29.89. $C_{23}H_{25}ON_3Br_2$. Calculated %: N 7.93; Br 30.19.

After running this reaction in acetonitrile with heating for 15 hours there was obtained (VI) in 60% yield.

Reaction of Harmine with Ethylene Bromide and Benzyl Chloride

1,2-Bis-(Py-N-1-methyl-7-methoxy-β-carbolinium)ethane dibromide (VIII). In the reaction of 1 g of harmine and 0.88 g of ethylene bromide in a mixture of 4 ml of anhydrous toluene and 4 ml of freshly distilled nitrobenzene, under conditions analogous to those for the preparation of (VI) there was obtained 1.2 g (83.3%) of product with m.p. 254-256° (from 80% aqueous dioxane; melting with decomposition).

Found %: Br 25.86, 26.03. $C_{28}H_{28}O_2N_4Br_2$. Calculated %: Br 26.05.

Py-N-benzyl-1-methyl-7-methoxy-β-carbolinium chloride. From 1 g of harmine and 1.2 g of benzyl chloride there was obtained analogously to the above reaction 1.3 g (81.2%) of the product with m.p. 246-248° (with decomposition) after recrystallization from 80% aqueous dioxane and drying at 110-120°.

Found %: Cl 10.33, 10.29; N 8.60, 8.76. $C_{20}H_{19}ON_2Cl$. Calculated %: Cl 10.46; N 8.56.

Compound (VIII) has two melting points: 104-118° and 246-248°, since it crystallizes with one molecule of water, but loses the latter on being heated to 110-120°.

SUMMARY

1. Two paths of synthesis were developed for unsymmetric bis-quaternary ammonium salts of the harmine series: a) reaction of harmine with dialkylaminoalkyl halides with the subsequent treatment of the product of the reaction with an alkyl halide, and b) reaction of harmine with ω-haloalkylammonium salts. The yields are are 55-75%.

2. The dependence of the hypotensive action on the structure in this series of compounds was discussed.

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**In Russian.

β-AMINOVINYL KETONES

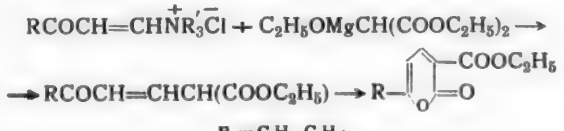
IX. SALTS OF TRIALKYL-(γ-OXOALKENYL)-AMMONIUM AS OXOVINYLATING AGENTS

L. I. Kudriashov and N. K. Kochetkov

As it was recently shown in our laboratory [1], trialkyl-(γ-oxoalkenyl)ammonium chlorides are formed in high yields in the reaction of β-chlorovinyl ketones with tertiary amines. The properties of these compounds, which are interesting from the point of view of clarification of the general problem of interaction of a nitrogen atom with a carbonyl group in the molecule of β-aminovinyl ketone [2-4], remain almost unknown to this data. In the present paper we described briefly the results obtained in the study of the reaction of these quaternary salts with ethoxymagnesium malonic ester. This problem is of interest for the comparison of the behavior of our compounds with their saturated isologs – Mannich base haloalkylates. The latter are known to enter reactions with compounds which have a mobile hydrogen in the presence of bases. This reaction, known under the name of Mannich-Robinson reaction, is used widely at this time in organic chemistry for synthesis [5]. In addition, most recently there was examined the reaction of the salts of oxoalkenylammonium type with salts of hydrocyanic acid [6] and it was shown that in this reaction there occurs a replacement of the ammonium groupings by the nitrile group. This reaction is also, by its nature, one of the variants of the Mannich-Robinson reaction.

We hoped that salts of trialkyl-(γ-oxoalkenyl)ammonium type would be convenient in the preparative sense as oxovinylating agents, which would replace the β-chlorovinyl ketones, used by us previously for the synthesis of γ-oxoalkenylmalonic esters [7] and 6-alkyl-3-carbethoxy-α-pyrones [8]. We studied the condensation of triethyl-(β-butyroylvinyl)ammonium and triethyl-(β-benzoylvinyl)ammonium chlorides, as well as trimethyl-(β-butyroyl vinyl)ammonium chloride, with ethoxymagnesiummalonic ester. The latter was selected as the metallic derivative since in the case of sodiomalonic ester we failed to isolate from the reaction products of any individual compounds, which fact is evidently connected with some additional complications [8]. The reaction was run by addition of the solution of the quaternary salt to the solution of ethoxymagnesiummalonic ester in alcohol, i.e., under conditions which are close to those of Mannich-Robinson synthesis. The product of the initial oxovinylation reaction – the corresponding γ-oxoalkenylmalonic ester – was not isolated but was used directly for the cyclization into the derivative of pyrone by thermal cyclization or by action of acetyl chloride as described by us previously [8]. This was more convenient for the evaluation of the degree of progress of the reaction since in contrast to the isolation of pyrones, the isolation of γ-oxoalkenylmalonic esters is complicated by certain difficulties. The 6-alkyl-3-carbethoxy-α-pyrones prepared by us were identified by hydrolysis to the corresponding acids [9].

The results thus obtained showed that the condensation proceeds but that the yields are low. Thus, the condensation of the salt of triethyl-(β-benzoylvinyl)ammonium type gave 6-phenyl-3-carbethoxy-α-pyrone in a 48% yield, while the salt of triethyl-(β-butyroylvinyl)ammonium type gave 6-propyl-3-carbethoxy-α-pyrone in a yield of only 15%; replacement of the triethyl-(β-butyroylvinyl)ammonium salt by the trimethyl-(β-butyroylvinyl)ammonium salt did not change the result although this change did occur in the reaction of oxoalkenylammonium salts with cyanides [6].



$R = C_3H_7, C_6H_5;$
$R' = CH_3, C_2H_5.$

It is evident that the results obtained by us are not of interest from the preparative viewpoint since it is more convenient to use β-chlorovinyl ketones for synthetic purposes [8, 9]. However, the reaction studied by us is interesting from the point of view of the principles, since it indicates that trialkyl-(γ-oxoalkenyl)ammonium salts, like haloalkylates of Mannich bases, are capable of exchange of their ammonium groups in typical reactions of nucleophilic substitution.

EXPERIMENTAL

1. Reaction of triethyl-(β-butyroylvinyl)-ammonium chloride with ethoxymagnesiummalonic ester. In a three-necked flask, provided with a stirrer, a dropping funnel and a reflux condenser, there was prepared in the conventional manner a solution of ethoxymagnesiummalonic ester from 6.18 g of magnesium, 45 ml of malonic ester and 60 ml of anhydrous alcohol; the solution was cooled with ice water and treated over 30 minutes with stirring with the previously prepared solution of the quaternary salt (to the solution of 27.3 g of propyl β-chlorovinyl ketone in 10 ml of absolute ether there was added with cooling 30 ml of triethylamine and after 2 hours the solidified mass was dissolved in 50 ml of boiling alcohol), after which the cooling was stopped and the mixture was heated on a boiling water bath for 12 hours. The crystals of triethylamine hydrochloride which precipitated on cooling were rapidly filtered off on a glass filter (after drying, m.p. 252°), and the filtrate was evaporated in vacuum; to the residue there was added 40 ml of glacial acetic acid, then 150 ml of water, the precipitated oil was extracted with toluene (3 × 30 ml), the toluene extracts were washed with 50 ml of 10% acetic acid and with water (2 × 50 ml), the toluene was distilled off, the residue was refluxed for four hours with 100 ml of acetyl chloride, the acetyl chloride excess was distilled off and the residue was distilled, collecting the fraction with b.p. 148° (2 mm) to 195° (4 mm). A second distillation gave 6-propyl-3-carbethoxy-α-pyrone; yield: 6.4 g (14.6%); b.p. 145-148° (1 mm), $n^{20}D$ 1.5180.

6-Propyl-α-pyrone-3-carboxylic acid was obtained by hydrolysis of 6-propyl-3-carbethoxy-α-pyrone; m.p. 113° (from alcohol). Literature data [9]: m.p. 113°.

2. Reaction of trimethyl-(β-butyroylvinyl)ammonium chloride with ethoxymagnesiummalonic ester. To the solution of 18.8 g of propyl β-chlorovinyl ketone in 10 ml of absolute ether there was added dropwise at 0°, the liquid trimethylamine obtained from 30 g of the hydrochloride, dried by passage through a column packed with solid potassium hydroxide. The apparatus contained a trap with freezing mixture (acetone + dry ice) which permitted the return of the evaporating trimethylamine into the reaction zone. The reaction mixture was left for two hours at 0°, then allowed to come to room temperature and the residues of trimethylamine and ether were removed in vacuum. The quaternary salt obtained in this manner was dissolved in 30 ml of anhydrous alcohol and added to the solution of ethoxymagnesiummalonic ester (prepared from 4.5 g of magnesium and 39 ml of malonic ester in 50 ml of anhydrous alcohol), then refluxed for 14 hours; the main bulk of alcohol was distilled off, to the residue there was added with cooling 20 ml of glacial acetic acid and the mixture was worked up as described in the previous experiment. The yield of 6-propyl-3-carbethoxy-α-pyrone was 4.8 g (16%); b.p. 145-148° (1 mm), $n^{20}D$ 1.5173.

6-Propyl-α-pyrone-3-carboxylic acid was obtained by hydrolysis of 6-propyl-3-carbethoxy-α-pyrone; m.p. 113° (from alcohol).

3. Reaction of triethyl-(β-benzoylvinyl)ammonium chloride with ethoxymagnesiummalonic ester. To the solution of ethoxymagnesiummalonic ester (prepared from 2.4 g of magnesium, 18 ml of malonic ester and 33 ml of anhydrous alcohol) there was added dropwise with cooling by means of ice water over 30 minutes 8 g of triethyl-(β-benzoylvinyl)ammonium chloride in 18 ml of anhydrous alcohol; the water bath was then heated over one hour to boiling and the refluxing was continued for two hours. After cooling, there was added 20 ml of glacial acetic acid and 10 ml of water, the resulting precipitated oil was extracted with toluene (3 × 30 ml), the toluene extracts were washed with water (2 × 25 ml), the toluene was distilled off and all materials boiling under 106° (10 mm; with slight decomposition) were removed from the residue in vacuum on an oil bath; the flask residue was dissolved in 10 ml of methanol after which the 6-phenyl-3-carbethoxy-α-pyrone was precipitated by water. The yield was 3.51 g (48%); m.p. 105° (from methanol). The literature data [10]: m.p. 105-106°.

SUMMARY

It was shown that trialkyl-γ-oxoalkenylammonium salts react with ethoxymagnesiummalonic ester, replacing the ammonium grouping by the malonic ester residue, i.e., they may serve as oxovinylating agents.

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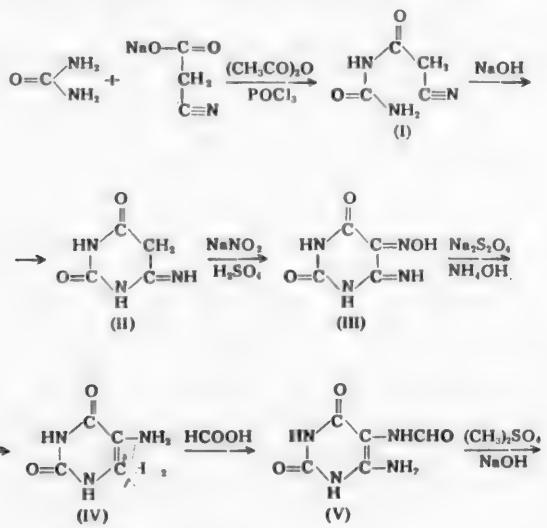
SYNTHESIS OF THEOPHYLLINE AND CAFFEINE FROM UREA AND SODIUM CYANOACETATE

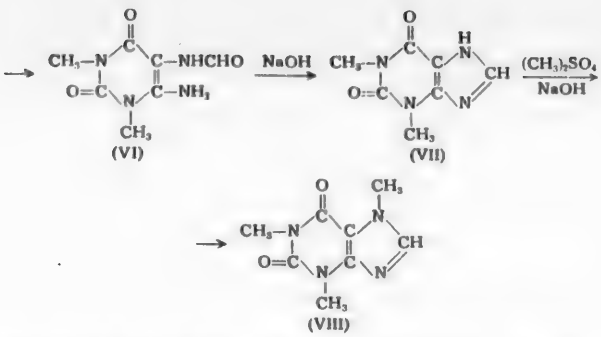
V. I. Khmelevskii and E. I. Abramova

The synthesis of theophylline (VII) and caffeine (VIII) from dimethylurea and cyanoacetic acid was performed for the first time by Traube [1]. In its initial form this method had only a theoretical interest. Later it was improved considerably by other workers [2-10]. However, the practical utilization of Traube's method was hindered by the fact that difficultly obtainable symmetric dimethylurea was used as the starting material for the synthesis of theophylline and caffeine. Gapner and Kreps [4] realized the synthesis of these compounds from methylurea, but this did not make the Traube method any more usable in the practical sense since monomethylurea still remains a difficultly accessible material. Bobranski and Synowiedski [5] replaced dimethylurea by urea in the preparation of theophylline and caffeine. The introduction of methyl groups into the pyrimidine or the imidazole rings of the above compounds was realized by these workers through methylation of the intermediate reaction products. For preparation of theophylline the iminobarbituric acid (II) was subjected to methylation, while for the preparation of caffeine, the formyl derivative of 4,5-diaminouracil (V) was methylated. An attempt to use the formyl derivative (V) for the preparation of theophylline as well, made by these authors, failed.

In working on the study of the methods of preparation of theophylline and caffeine, we studied in detail the process of methylation of the formyl derivative of 4,5-diaminouracil (V). Here it was established that methylation of compound (V) by two moles of dimethyl sulfate, taken in slight excess at 25-27° and pH 8.5-9 gave 1,3-dimethyl-4-amino-5-formylaminouracil (VI) in almost quantitative yield.* This permitted us to realize the synthesis of theophylline and caffeine according to the scheme shown below:



*According to the German patent [11], the formyl derivative of 4,5-diaminouracil is methylated to 1,3-dimethyl-4-amino-5-formylaminouracil by means of methyl iodide under pressure.



As it is evident from this scheme, cheap urea and sodium cyanoacetate are used as the starting materials for the synthesis. In case of the preparation of caffeine (VIII), theophylline (VII) becomes an intermediate product of the synthesis.

In completion of this work, besides the study of the process of methylation of the formyl derivative of 4,5-diaminouracil, we studied the methods of preparation of various intermediate products of synthesis of theophylline. As the result of this the yields were considerably improved and the quality of the intermediate products was improved.

Nitrosation of iminobarbituric acid (II) was run precisely under the conditions described in the literature [12].

The preparation of cyanoacetylurea (I) – the first intermediate product in the synthesis of theophylline – was run by us according to the method of Hepner and Frenkenberg [3], which these authors had used in the preparation of phenylmethylcyanoacetylurea. This permitted us to prepare cyanoacetylurea of good quality in yields of 82-84%.

Cyclization of cyanoacetylurea (I) into iminobarbituric acid (II) was run in a solution of sodium hydroxide. Several methods of cyclization of cyanoacetylurea into iminobarbituric acid have been described in the literature [1, 5, 12]. During the experimental verification it appeared that none of them afford a product of good quality in a satisfactory yield. The best yield of iminobarbituric acid (II) was obtained by us in the treatment of cyanoacetylurea (I) for three hours with 40% solution of sodium hydroxide at 25°.

Reduction of iminovyaluric acid to 4,5-diaminouracil was performed with sodium hydrosulfite according to the technique which was used by Bogert and Davidson [13] for the reduction of 5-nitrouracil.

Considerable improvements were also made in the stages of preparation of the formyl derivative of 4,5-diaminouracil, the sodium salt of theophylline and its isolation from the reaction mixture.

All this permitted us to increase very considerably the yield of theophylline and caffeine. In calculation on the initial sodium cyanoacetate, the yield of theophylline was 50%. In methylation of the sodium salt of theophylline with dimethyl sulfate there was obtained a 94-95% yield of caffeine.

EXPERIMENTAL

Preparation of cyanoacetylurea (I). In a three-necked flask with ground glass joints, provided with a stirrer, thermometer and a condenser, there was placed 90 g of 40% (or 36 g 100%) well dried sodium cyanoacetate and 40 ml of glacial acetic acid. To the resulting thick mixture there was added with stirring 10 ml of phosphorus oxychloride. The reaction mixture liquefied during this operation and the temperature rose to 50-60°. After addition of the entire amount of the phosphorus oxychloride at 50°, there was added 20 g of urea and 55 ml of acetic anhydride. (During the addition of acetic anhydride a small exothermic effect is observed sometimes). The contents of the flask were heated to 65-67° and kept at this temperature for two hours. Then the stirrer was replaced by a capillary tube and the reflux condenser by a downward condenser, after which the mixture of acetic anhydride and acetic acid was distilled in vacuum at a temperature not more than 67°. To the remaining solid residue there was added 100 ml of water and, after one hour's standing and replacing the capillary tube by the stirrer, the reaction mixture was stirred until a homogeneous suspension resulted. The undissolved precipitate of cyanoacetylurea was filtered off and washed thoroughly with water until the acid test to litmus disappeared. The resulting product was dried at 100-110°. The yield of cyanoacetylurea was 35.9 g (84.1%). The m.p. of the technical grade product

was 203-206°. After recrystallization from water: m.p. 208-211° [14, 15].

Cyclization of cyanoacetylurea into iminobarbituric acid (II). Into a three-necked flask, provided with a stirrer and a thermometer, there was placed 90 ml of 40.9% solution of sodium hydroxide and over one hour at a the temperature not in excess of 20-25° there was gradually added 30 g of cyanoacetylurea with m.p. 200-203°. After all the cyanoacetylurea had been added, the flask contents were maintained at 20-25° for 2.5 hours. The initially thick and difficultly stirrable heterogeneous mass became more fluid gradually and at the end of the treatment it was completely homogeneous. The resulting sodium salt of iminobarbituric acid was neutralized with 1:1 hydrochloric acid with cooling to a neutral test with Bromthymol blue. After 3-5 hours standing, the precipitated iminobarbituric acid was filtered off, pressed well and used in this state for the conversion to iminovyaluric acid, considering that the yield of iminobarbituric acid was theoretical, i.e., 30 g.

Preparation of iminovyaluric acid (III). Nitrosation of iminobarbituric acid (II), prepared in the preceding experiment, was run by the technique of Biltz and Schmidt [12]. From 30 g of compound (II) there was obtained 35.6 g (84.8%) of the sodium salt of iminovyaluric acid.

Reduction of iminovyaluric acid to 4,5-diaminouracil (IV). To the suspension of 35.6 g of sodium salt of iminovyaluric acid in 560 ml of water there was added 24.6 ml of 19.7% solution of ammonia and 172 g of sodium hydrosulfite (the medium was basic to phenolphthalein). After addition of the sodium hydrosulfite, the reaction mixture was heated on a water bath at 55° for 15 minutes, after which the bath was heated to boiling and the reaction mixture was kept on the boiling water bath for ten minutes. The reaction mixture became totally colorless. The resulting precipitate was filtered off, after cooling to 10°, washed with water to remove all odor of sulfur compounds and dried at 60-70°. The yield of technical grade (96%) 4,5-diaminouracil was 28.6 g (96.8%).

Preparation of 4-amino-5-formylaminouracil (V). To the suspension of 28.6 g of 4,5-diaminouracil in 200 ml of water there was added 17 ml of 85% formic acid. The resulting mixture was refluxed for one hour, after which it was allowed to stand for two hours at room temperature. The resulting precipitate of the formyl derivative was filtered off, washed with water and dried at 60-70°. The yield was 31.6 g (91.3%).

Preparation of theophylline (VII). a) Methylation of the formyl derivative of 4,5-diaminouracil. The formyl derivative of 4,5-diamonouracil (31.6 g) was suspended in 190 ml of water. To the resulting suspension there was added with energetic stirring 54.6 g of dimethyl sulfate in one portion after which 72 ml of 6 N solution of sodium hydroxide was added gradually, maintaining the pH of the solution at 8.5-9 during the process of methylation at 25-27°. The addition of alkali usually required 60-75 minutes. The formyl derivative of 4,5-diaminouracil passed partially into solution during the methylation process and simultaneously with this there occurred the precipitation of the methylated product. At times a complete solution of the precipitate was observed and the solution remained clear for 10-15 minutes after which a rapid thickening of the reaction mixture occurred. A colorless precipitate (needles) of 1,3-dimethyl-4-amino-5-formylaminouracil formed. After the consumption of alkali had terminated (for 5-10 minutes the pH of the medium remained without change), the mixture was kept at 25-27° for one hour, adding (in case of disappearance of the alkaline reaction to phenolphthalein) an additional amount of alkali. Usually after one hour's stirring, the pH of the medium does not change.

b) Transformation of the formyl derivative of 1,3-dimethyl-4,5-diaminouracil into theophylline. To the reaction mixture obtained in the preceding experiment there was added 31.6 ml of 6 N solution of sodium hydroxide, 71 g of sodium chloride and the solution was heated on a water bath. At 45-50° there took place a complete dissolution of the precipitate, while at 55-60° there began to precipitate the sodium salt of theophylline. The reaction mixture was kept for ten minutes at 80-95° and allowed to stand for 10-12 hours. The precipitate of the sodium salt of theophylline was filtered off after cooling of the reaction mixture to 10°, and was washed with a saturated solution of sodium chloride, after which it was dissolved in 400 ml of water with heating on a boiling water bath. Carbon was added to the resulting solution and after 15 minutes of heating on a boiling water bath the mixture was filtered. To the hot colorless solution there was added with stirring 100 g of sodium chloride. Sodium salt of theophylline precipitated and this, after 2-3 hours of standing at room temperature, was cooled to 10°, filtered, pressed well on the filter and suspended in 25 ml of water. The resulting suspension was neutralized with 25 ml of hydrochloricaacid (1:1) until neutral to Bromthymol blue and to Congo red. The resulting colorless precipitate of theophylline was filtered off after 3-4 hours standing at room temperature and dried at

120-125°. The weight of theophylline was 29 g (92%); m.p. 263-265°. After recrystallization from 5-6 parts of water, the weight was 26 g (82%); m.p. 268-170° (mixed m.p. with authentic theophylline was 269-270°).

Found %: N 31.16. $C_7H_8O_2N_4$. Calculated %: N 31.09.

Methylation of theophylline to caffeine (VIII). Into a three-necked flask, provided with a stirrer, a thermometer and a reflux condenser, there was placed 20 g of theophylline, 60 ml of water and 15 ml of 32.2% solution of sodium hydroxide. The flask contents thickened considerably during this operation. To the resulting sodium salt of theophylline there was gradually added with intensive stirring 11.8 ml of dimethyl sulfate, maintaining the temperature of the reaction mixture during methylation within 32-35°. The precipitate of the sodium salt of theophylline dissolved completely toward the end of methylation and almost immediately the caffeine precipitated. The reaction mixture was kept at 40-45° for one hour, maintaining the alkaline reaction to Bromthymol blue, after which it was heated to 90° and left at room temperature for 5-10 hours. The reaction mixture was then cooled to 5°-0°, the precipitate of caffeine was filtered off, washed on the filter with a small volume of ice water and dried at 110-120°. The weight of dry caffeine was 20.4 g. The m.p. of the technical grade product was 231-233°. After recrystallization from 3 parts of water with addition of activated charcoal, there was obtained 18.6 g of pure caffeine with m.p. 232-235°. From the mother liquor and the filtrate from the recrystallization there was obtained by extraction and a subsequent purification an additional 1.6 g of pure caffeine. The total yield of caffeine was 20.2 g (94%). The mixed m.p. with authentic caffeine was 232-234°.

SUMMARY

1. Theophylline and caffeine were prepared in 50% yield from urea and sodium cyanoacetate. The synthesis of these compounds was done by one reaction scheme.

2. The methods of preparation of intermediate products in the synthesis of theophylline – cyanoacetylurea, iminobarbituric acid etc. – were improved. The possibility of methylation of the formyl derivative of 4,5-diaminouracil with dimethyl sulfate in an alkaline medium to 1,3-dimethyl-4-amino-5-formylaminouracil was indicated.

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PREPARATION OF THEOPHYLLINE AND CAFFEINE FROM URIC ACID

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Several methods of preparation of caffeine (VI) and theophylline (V) from uric acid (I) have been described in the literature.

In 1899-1901 the workers of the Bayer firm had accomplished the transformation of uric acid into 8-methylcaffeine [1, 2]. In chlorination of 8-methylcaffeine [3, 4] and the subsequent hydrolysis of the tri- and tetra-halo derivatives formed thereby [5], there occurs a removal of one or two methyl groups and, accordingly, there is formed either caffeine or theophylline. E.Fischer prepared 8-chlorocaffeine from uric acid [6-8], the former being used subsequently for the preparation of theophylline [9-11] and other derivatives of xanthine.

In 1950-1953 Bredereck and co-workers published several papers on the utilization of uric acid for the preparation of caffeine, theophylline and other derivatives of xanthine. According to the data obtained by these authors, xanthine is formed on heating uric acid with formamide, while methylation of xanthine with dimethyl sulfate in an alkaline medium yields caffeine [12]. In later papers [13, 14] Bredereck and co-workers used the triacetyl derivative of 4,5-diaminouracil as an intermediate product for the preparation of caffeine and theophylline, this intermediate being prepared by them by the reaction of uric acid with acetic anhydride in the presence of pyridine.

Only one of the published methods from the literature has found a practical application for the preparation of theophylline and caffeine from uric acid, this method utilizing 8-methylcaffeine as an intermediate product. However even this method has material defects, despite the improvements developed by I. T. Strukov and L. S. Diskina [15], as well as E. S. Golovchinskaia [16], the defects which prevent the wide use of uric acid for the preparation of the indicated products. At the same time the use of uric acid for an industrial synthesis of medicinal agents of the purine series has a first rate importance since uric acid is an available product and may be obtained in any amount from the wastes of poultry husbandry – hen manure.

In a search for a simpler method of preparation of caffeine and theophylline we started with 4,5-diacetylaminouracil (II), the method of preparation of which from uric acid had been developed by the present authors [17]. Substance (II) on treatment with alkali may cleave one or two acetyl groups and be transformed into 4-amino-5-acetylaminouracil (VII) or into 4,5-diaminouracil (VIII).

Several methods of hydrolysis of 4,5-diacetylaminouracil (II) to the monoacetyl derivative [13, 18] and 4,5-diaminouracil [13, 19] are known. During the experimental verification it was established that all of them yield final products of poor quality and, owing to this, are unsuitable for practical utilization.

A detailed study of the conditions of hydrolysis of the diacetyl derivative (II) showed that the acetyl group in position 4 is especially readily cleaved. On heating 4,5-diacetylaminouracil on a water bath for one hour with a dilute solution of aqueous ammonia (approximately 0.9 N) used in slight excess over the theoretical amount, there is formed 4-amino-5-acetylaminouracil (VII) in yield of 93-95% [20]. On heating 4-amino-5-acetylaminouracil on a water bath for two hours with 6-10 N solution of sodium hydroxide, both acetyl groups are cleaved and there is obtained 4,5-diaminouracil, which is isolated from the reaction mixture in the form of its sulfate (VIII) on acidification with sulfuric acid.

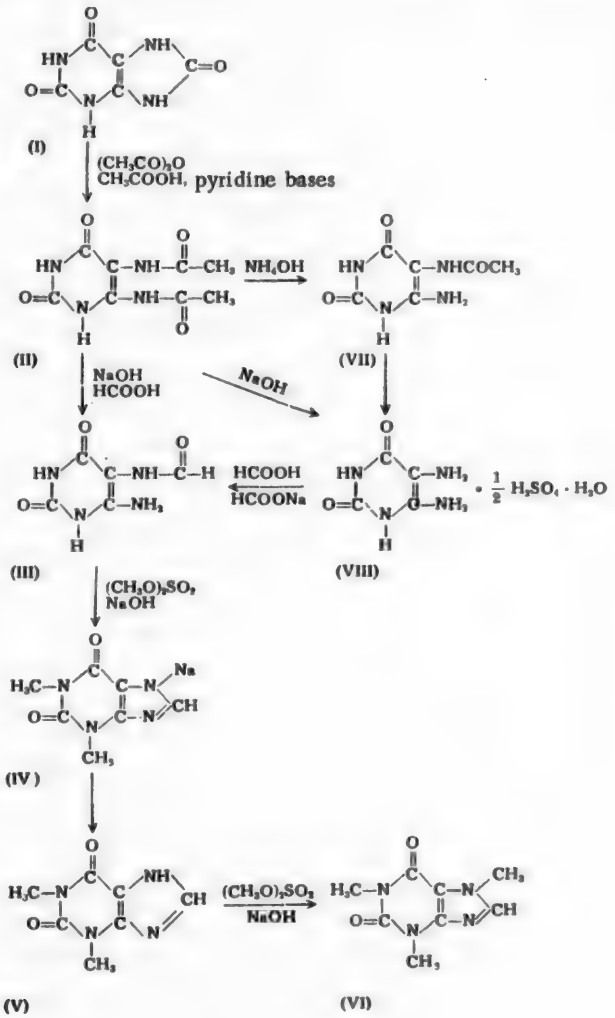
4,5-Diaminouracil may also be obtained from the monoacetyl derivative (VII). In contrast to the diacetyl derivative (II), which is hydrolyzed to 4,5-diaminouracil only in alkaline medium, the monoacetyl derivative

(VII) may be hydrolyzed to 4,5-diaminouracil not only in alkaline but also in acidic medium [13].

As shown by our experiments, the monoacetyl derivative (VII) is hydrolyzed by a solution of sulfuric acid in methyl alcohol; hereby there is formed the acid sulfate of 4,5-diaminouracil with yields of 93-95%. A somewhat lower yield of the sulfate of 4,5-diaminouracil (VIII) is obtained after a brief heating (10-15 minutes) of the monoacetyl derivative with a large excess of 2 N aqueous solution of sulfuric acid on a water bath.

The sulfate of 4,5-diaminouracil (VIII) obtained through the use of the alkaline or the acidic hydrolysis, is converted into the formyl derivative of 4,5-diaminouracil (III) by heating with an aqueous solution of sodium formate and a small amount of formic acid. This compound (III) yields the sodium salt of theophylline (IV) on methylation with dimethyl sulfate and a subsequent cyclization in an alkaline medium [21].

Duration the preparation of the formyl derivative of 4,5-diaminouracil (III) there is no necessity for the isolation of the sulfate of 4,5-diaminouracil. If the reaction mixture formed after the hydrolysis of the diacetyl derivative with sodium hydroxide is acidified with formic acid and the resulting mixture is boiled for one hour, the end product of the reaction is the formyl derivative of 4,5-diaminouracil (III). The excess alkali after the hydrolysis may be also neutralized with hydrochloric acid and the formic acid added only in an amount needed for the formylation of the 4,5-diaminouracil. The entire process of transformation of uric acid into theophylline and caffeine may be shown by the following scheme:



In working along this scheme the yield of theophylline reaches about 45-46% calculated on the original uric acid. The yield of caffeine in methylation of theophylline with the dimethyl sulfate reaches 90-94%.

EXPERIMENTAL

Preparation of diacetyl derivative of 4,5-diaminouracil (II). Into a three-necked round bottomed flask with ground glass joints, with 750 ml capacity, provided with a stirrer, a thermometer and a reflux condenser, there was placed 100 g of 92-95% uric acid, 150 ml of acetic anhydride, 180 ml of acetic acid (glacial) and 100 ml of pyridine bases boiling in the interval of 126-138°. The flask contents were refluxed, with constant stirring, on an oil bath (the bath temperature was 155-160°) until the cessation of evolution of carbon dioxide, which was completed after 3.5-4 hours. To the reaction mixture was added 10 ml of water and the heating was continued for 30 minutes. The resulting diacetyl derivative of 4,5-diaminouracil was filtered off after cooling, thoroughly pressed free of mother liquor, suspended in 130-150 ml of water and reflitered. This operation was repeated twice. The thus washed product was dissolved without drying in 22.5 fold (relative to the weight of uric acid) amount of water with heating and the mixture was filtered from the water insoluble 8-methylxanthine. To the filtrate there was added 2 g of activated carbon, the solution was boiled for 3-5 minutes and filtered once again. The filtrate was cooled to 5-10° and the precipitated diacetyl derivative was filtered off and dried at 100-120°. Its weight was 84 g. The mother liquor, obtained from the crystallization of the diacetyl derivative, was evaporated on a water bath until crystallization began. The precipitate was filtered off and dried at 100-120°. The weight of the diacetyl derivative isolated from the mother liquor was 9.4 g. The total yield was 93.4 g (75%).

The weight of dry technical grade 8-methylxanthine containing 60% pure product was 14.8 g. Thus, the yield of the diacetyl derivative of 4,5-diaminouracil (with allowance for the 8-methylxanthine obtained) is about 85% calculated on 100% uric acid.

Preparation of 4-amino-5-acetylaminouracil (VII). Into a three-necked flask provided with a stirrer, a thermometer and a reflux condenser there was placed 30 g of 4,5-diacetylaminouracil and 120 ml of water. The flask contents were heated with intensive stirring on a boiling water bath and 60 ml of 2.5 N aqueous ammonia was added at 93-95°. At first there occurred a complete solution of the diacetyl derivative of 4,5-diaminouracil, after which there formed a precipitate of the monoacetyl derivative of 4,5-diaminouracil. After one hour of heating on the boiling water bath, the flask contents were cooled to room temperature and acidified with dilute (1 : 1) hydrochloric acid to an acid reaction with litmus. The resulting precipitate of the monoacetyl derivative of 4,5-diaminouracil was filtered off, washed thoroughly with water until neutral to litmus and dried at 100-120°. The weight of technical grade product was 20 g (94.5%).

Preparation of 4,5-diaminouracil sulfate (VIII). a) By hydrolysis of 4,5-diacetylaminouracil (II) in alkaline medium. Into a three-necked flask provided with a stirrer and a reflux condenser there was placed 30 g of the diacetyl derivative of 4,5-diaminouracil and 180 ml of 6 N sodium hydroxide. The resulting transparent solution of the sodium salt of the diacetyl derivative was heated for two hours on a boiling water bath. Then, there was added to the reaction mixture 180 ml of water, the whole was cooled to 40° and neutralized with 28 ml of 1 : 1 sulfuric acid until acid to Congo red. The temperature was maintained below 50° during the neutralization. The reaction mixture was cooled to 25°, the resulting precipitate of 4,5-diaminouracil sulfate was filtered off and washed with water until no longer acid to litmus. The weight of the product, dried at 60-70°, was 24 g (87%).

b) By hydrolysis of 4-amino-5-acetylaminouracil with sulfuric acid in methyl alcohol. Into a three-necked flask, provided with a stirrer with a mercury seal, a reflux condenser with a calcium chloride tube and a dropping funnel, there was placed 23 g of 4-amino-5-acetylaminouracil and 230 ml of methyl alcohol dried over unquenched lime. With intensive stirring there was gradually added to the resulting suspension 23 ml of concentrated sulfuric acid and the mixture was refluxed for five hours. After cooling, the precipitate was filtered off, washed several times with alcohol and dried at 50-60°. The yield of 4,5-diaminouracil acid sulfate was 27.8 g (93%).

c) By hydrolysis of 4-amino-5-acetylaminouracil with aqueous solution of sulfuric acid. To a suspension of 15 g of 4-amino-5-acetylaminouracil in 750 ml of water, heated on a water bath to 93-95°, there was added with intensive stirring a hot solution of 56 ml of concentrated sulfuric acid in 150 ml of water. The reaction mixture was kept on a boiling water bath for ten minutes from the instant of complete solution of the precipitate, after which it was cooled to room temperature. The colorless crystalline precipitate was filtered off, washed thoroughly with water until no longer acid to Congo red and dried at 50-60°. The yield of diaminouracil sulfate was 11.9 g (70%).

Preparation of 4-amino-5-formylaminouracil (III). a) From 4,5-diaminouracil sulfate. A mixture of 24 g of diaminouracil sulfate, 8 g of sodium formate, 3.5 ml of 85% formic acid and 168 ml of water was refluxed for one hour in a flask provided with a reflux condenser and a stirrer. The resulting precipitate was filtered off after cooling to room temperature and was thoroughly washed with water. The yield of the dry formyl derivative was 19.2 g (93.4%).

b) From 4,5-diacetylaminouracil. Into a three-necked flask of 500 ml capacity, provided with a stirrer, a thermometer and a reflux condenser, there was placed 114 ml of 10 N sodium hydroxide which was then heated on a boiling water bath to 93-95°. At this temperature there was added 30 g of the diacetyl derivative of 4,5-diaminouracil and the resulting solution was heated on the boiling water bath for two hours. After this period there was added 66 ml of water, the flask contents were cooled to 40° and treated rapidly with 79.5 ml of 85% formic acid. The resulting mixture was refluxed for one hour with continuous stirring after which it was allowed to cool gradually to room temperature over 2-3 hours. The resulting precipitate of 4-amino-5-formylaminouracil was filtered off, washed thoroughly with water and dried at 60-70°. The yield was 18.8 g (79.5%).

It is possible to acidify the reaction mixture after hydrolysis with concentrated hydrochloric acid instead of formic acid. In this case the neutralization is made to acid reaction to Congo red (about 114 ml) at 5-10°. The excess acidity is removed with 10 N sodium hydroxide (about 2.4 ml) until neutral to Congo red. Then there was added to the reaction mixture 14 ml of 10 N sodium hydroxide and 15 ml of 85% formic acid and the formylation process is carried out as in the case with neutralization by means of formic acid.

Preparation of theophylline (V) and caffeine (VI). Methylation of the formyl derivative of 4,5-diaminouracil with dimethyl sulfate and the cyclization of the resulting 1,3-dimethyl-4-amino-5-formylaminouracil into theophylline and caffeine were performed under the conditions described for the synthesis of theophylline from urea and sodium cyanoacetate [22]. From 18.8 g of the formyl derivative of 4,5-diaminouracil there was obtained 12.5 g of theophylline (67%). M.p. 268-270° (literature data: m.p. 269° [14]).

Found %: N 31.14, 31.22. $C_7H_8O_2N_4$. Calculated %: N 31.09.

From 12.6 g of theophylline there was obtained 12.7 g of caffeine with m.p. 232-235° (literature data: m.p. 234-236° [23]).

SUMMARY

1. There was described a method of preparation of theophylline and caffeine from uric acid utilizing as an intermediate product 4,5-diacetylaminouracil.

2. The conditions of preparation of the following intermediate products of the synthesis of theophylline and caffeine are given: 4,5-diacetylaminouracil (II), 4-amino-5-acetylaminouracil (VII), 4,5-diaminouracil sulfate (VIII) and 4-amino-5-formylaminouracil (III).

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A STUDY IN THE FIELD OF POLYCYCLIC QUINONES

III. REACTION OF 1-HALOANTHRAQUINONE WITH SECONDARY ALKAROMATIC AMINES

N. S. Dokunikhin and T. N. Kurdiumova

It is known that the halogen atom in α-halo substituted derivatives of anthraquinone is replaced relatively readily by residues of primary aliphatic or aromatic amines [1]. The secondary aliphatic amines react with 1-haloanthraquinone under approximately the same conditions as do the primary amines [2]. Diphenylamine does not react with 1-chloroanthraquinone, but does so with 1-iodo- and 1-bromoanthraquinones at a temperature above 200°, forming 1-N,N-diphenylaminoanthraquinone [3]. We failed to find in the literature any data on the reaction of 1-halo substituted anthraquinones with secondary alkaromatic amines and on the description of properties of N,N-alkylaryl substituted 1-aminoanthraquinones.

We showed in preliminary experiments that 1-chloroanthraquinone does not react with methylaniline under the usual conditions of preparation of arylamino derivatives of anthraquinone, i.e., in boiling butanol in the presence of copper catalyst and a basic reagent [4]. Over 95% of the original 1-chloroanthraquinone was isolated from the reaction mixture. However, after heating 1-chloroanthraquinone in excess methylaniline to 170-175° for 7 hours in the presence of potassium acetate and copper acetate and metallic copper there was isolated from the reaction products some 47.8% of 1-N,N-methylphenylaminoanthraquinone, 11% of 1-anilinoanthraquinone and 28.8% of anthraquinone. With ethylaniline under these conditions there was obtained 1.0% of 1-N,N-ethylphenylaminoanthraquinone, 30.8% of anilinoanthraquinone and 55.5% of anthraquinone.

The formation of anthraquinone as the result of heating 1-chloroanthraquinone in nitrobenzene with potassium acetate and copper compounds had been observed in 1912 by Ullmann and Minajeff [5] and later by Bradley [6]. A recent study [7] has been devoted to the dehalogenation of 1-chloroanthraquinone under similar conditions, in which there were examined the effects of temperature, the nature of the solvent and of the acid-binding reagent on the degree of conversion and on the composition of the reaction products. According to these data the replacement of potassium acetate by potassium carbonate leads to a considerable decrease of the rate of dehalogenation and the reaction product is not anthraquinone but 1,1'-dianthraquinonyl. According to our observations, the reaction of 1-chloroanthraquinone with methylaniline is also retarded by the presence of potassium carbonate. As the result of heating 1-chloroanthraquinone with excess methylaniline at 190° for 15 hours in the presence of potassium carbonate and metallic copper, there was isolated 33.5% of unreacted 1-chloroanthraquinone. After 30 hours of heating there was found among the reaction products: 26.7% of 1-N,N-methylphenylaminoanthraquinone, 10.6% of 1-anilinoanthraquinone and 51.5% of unpigmented substance which was free of halogen and which did not melt at 420°. This substance gave an intensely green color with concentrated sulfuric acid, while with metallic opper it gave the characteristic qualitative test for 1,1'-dianthraquinonyl [6]. However, contrary to the data [7], the character of the product of dehalogenation does not depend only on the selection of the acid-binding reagent. In the reaction of 1-bromoanthraquinone with N,N-dicyclohexylamine, with potassium carbonate and copper, there was isolated 37.5% of anthraquinone which did not contain even traces of 1,1'-dianthraquinonyl.

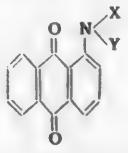
Considering the closeness of the natures of aniline and methylaniline as solvents, it was interesting to compare under the same conditions the degrees of dehalogenation of 1-chloroanthraquinone in its reaction with primary and secondary amines. It turned out that from the reaction products of 1-chloroanthraquinone with aniline it is possible to isolate, along with anilinoanthraquinone, only 1.5% of anthraquinone, which fact is evidently explained by the considerably greater rate of the competing reaction of arylamination by the primary amine. One

may expect that owing to the greater mobility of the bromine atom one might reach a higher yield of 1-N,N-methylphenylaminoanthraquinone by starting with 1-bromoanthraquinone. However, in this case the rate of dehalogenation rises to an even greater degree. There was isolated from the reaction mixture some 68% of anthraquinone.

Dealkylation in the reaction of 1-chloroanthraquinone with secondary aliphatic amines (except for dimethylamine) was recently observed by Bradley [8]. In our experiments during the reaction of chloroanthraquinone with N-alkylanilines there also took place the cleavage of the methyl group. As indicated above, the yield of 1-anilinoanthraquinone comprises some 11% in the case of reaction with methylaniline, and some 30.8% – with ethylaniline. The formation of 1-anilinoanthraquinone cannot be explained by a cleavage of the alkyl residue from 1-N,N-alkylphenylaminoanthraquinone. Under the conditions of the reaction (in the presence of potassium acetate, excess methylaniline, metallic copper and its salts) only traces of 1-anilinoanthraquinone were formed from 1-N,N-methylphenylaminoanthraquinone in 8 hours of heating at 175°. One may suppose that the anilinoanthraquinone is formed from the primary amine which forms in the reaction mixture as the result of disproportionation of alkylaniline with simultaneous formation of dialkylaniline. This supposition is confirmed by the fact that in the reaction of 1-chloroanthraquinone with ethylaniline (taken in amount equal to 140% of theoretical) in the presence of a large amount of diethylaniline the yield of anilinoanthraquinone was but 3.5 instead of 30.8% obtained with a large excess of ethylaniline.

1-N,N-Alkylphenylamino derivatives of anthraquinone are readily crystallizing substances which are soluble a majority of organic solvents. They differ from 1-anilinoanthraquinone by the deeper purple color of solutions and by smaller mobility and deeper color of the absorptional layer in chromatographic separation on aluminum oxide. In the following table there are given the data which characterize the absorption of light by carbon tetrachloride solutions of N-alkyl, N-aryl-, N,N-diaryl- and 1-N,N-alkylphenylaminoanthraquinones. 1-N,N-Diphenylaminoanthraquinone which had not been characterized sufficiently well in the literature [3], was synthesized by us from diphenylamine and 1-bromoanthraquinone in the presence of potassium carbonate and metallic copper. In its properties it is very close to the above described N,N-alkylaryl substituted derivatives.

Light Absorption by Solutions in CCl_4 of Compounds of General Formula:



Substituents		λ'_{max} (mμ)	ε′	λ''_{max} (mμ)	ε″	λ'''_{max} (mμ)	ε‴
X	Y						
H	CH_3	315	5620	—	—	495	6850
CH_3	CH_3	319	5770	388.5 409	1450 1540	495.5	4940
H	C_6H_5	320.5	8750	—	—	502.5	7300
CH_3	C_6H_5	320	5800	372	3450	532	2550
C_2H_5	C_6H_5	320	5920	372	2840	537.5	1970
C_6H_5	C_6H_5	320	8760	380	4970	535.5	2860

A comparison of the data from the measurements of light absorption shows that the replacement of hydrogen at the nitrogen atom by alkyl or aryl residue in 1-anilinoanthraquinone causes a shift of the principal absorption maximum by 30-35 m toward the longer wave part of the spectrum. Simultaneously, the intensity of absorption in the visible region drops sharply, which fact is often observed in noncoplanar molecules. The characteristic of light absorption by secondary and tertiary amines is the presence of an additional absorption band in the region of 370-380 m found among the tertiary amines.

EXPERIMENTAL

Monoalkylanilines. Both methyl- and ethylanilines were treated with phthalic anhydride prior to distillation in order to remove the admixture of primary amine (according to B. A. Porai-Koshits [9]). The content of monomethylaniline was 100% and that of monoethylaniline was 93.25% in the distilled amines. The latter product contained 6.5% of diethylaniline.

1-N,N-Methylphenylaminoanthraquinone. 1-Chloroanthraquinone (12.1 g) was heated with 40 ml of methylaniline, 5.5 g of potassium acetate, 0.12 g of powdered metallic copper and 0.12 g of copper acetate for seven hours at reflux with good stirring. The color of the reaction mixture changed from yellow to raspberry. The precipitate (I) which formed on cooling was filtered off, washed with methyl alcohol, dilute hydrochloric acid and water, and was then dried. From the resulting lightly colored precipitate (3.65 g) there was isolated by solution in concentrated sulfuric acid with subsequent dilution of the solution to the concentration of 82%, 3 g (28.8%) of anthquinone with m.p. 278-280°. The latter was identified by the absence of depression in mixed melting point with an authentic sample. By further dilution of the sulfuric acid solution there was isolated 0.53 g of deep red substance in which there was established, by chromatographic analysis on aluminum oxide, the presence of 10% of 1-methylphenylaminoanthraquinone and 20% of 1-anilinoanthraquinone.

The liquid remaining after the separation of precipitate (I), with the methyl alcohol used for washing the precipitate (I), was poured into dilute hydrochloric acid with energetic stirring and external cooling. The resulting precipitate (II) was filtered off, washed with dilute hydrochloric acid and water, and was dried. The yield of crude product was 9.73 g. Precipitate (II) was dissolved in carbon tetrachloride. By chromatographic analysis of this solution there was shown the presence in it of 1-anilinoanthraquinone (15.8%) and 1-methylphenylaminoanthraquinone (76.9%). Thus the total yield of 1-N,N-methylphenylaminoanthraquinone was 7.5 g (49.8%) and that of 1-anilinoanthraquinone was 1.64 g (11%). 1-Anilinoanthraquinone isolated by chromatography had m.p. 139-141°. It was identified by the absence of depression in mixed melting point with an authentic sample of 1-anilinoanthraquinone and by the coincidence of the absorption curves for both samples in carbon tetrachloride solution. 1-N,N-Methylphenylaminoanthraquinone had m.p. 130-131° (from alcohol).

Found %: C 80.23, 80.07; H 5.00, 4.82; N 4.28, 4.35. $C_{21}H_{15}O_2N$. Calculated %: C 80.52; H 4.75; N 4.47.

1-N,N-Ethylphenylaminoanthraquinone. A mixture of 12.1 g of 1-chloroanthraquinone, 40 ml of ethylaniline, 5.5 g of potassium acetate, 0.42 g of metallic copper and 0.12 g of copper acetate was heated under reflux with good stirring for 7 hours at 170-175°. By filtration of the reaction mixture after cooling and subsequent treatment described above, there was isolated 5.68 g (54.5%) of anthraquinone with m.p. 278-280°. By means of chromatographic analysis there was found in the mixture 0.1 g (0.6%) of 1-N,N-ethylphenylaminoanthraquinone with m.p. 140-143° (from alcohol) and 4.6 g (30.8%) of 1-anilinoanthraquinone.

Found %: C 80.07, 79.86; H 5.20, 5.07; N 4.64, 4.78. $C_{22}H_{17}O_2N$. Calculated %: C 80.73; H 5.20; N 4.28.

Isolation of anthraquinone from a mixture with 1-anilino- and 1-N,N-methylphenylaminoanthraquinone. A sample of 4 g of dry product prepared by filtration of the reaction mixture with a subsequent washing with alcohol and dilute hydrochloric acid, was dissolved in 50 g of 94% sulfuric acid with stirring. To the resulting solution there was added over 1.5 hours with stirring enough dilute sulfuric acid (48.50%) to gradually lower the concentration of the solution to 82%. During this all the anthraquinone precipitated in the form of the sulfate (colorless needles). The mixture was allowed to stand for several hours for completion of crystallization, after which it was filtered through a porous glass filter, washed with 5-10 ml of 82% sulfuric acid, and the precipitate was pressed well on the filter and then was transferred with the aid of a large volume of water into a beaker. The resulting somewhat gray anthraquinone was filtered quantitatively, dried and weighed.

The sulfuric acid solution (acid concentration 82%) was poured into a large volume of water and the precipitated dark red mixture of 1-anilino- and 1-N,N-alkylphenylaminoanthraquinone was filtered off. The mixture may be separated by the chromatographic method. From an artificial mixture of 2 g of anthraquinone and 2 g of 1-anilinoanthraquinone it was possible to remove by this method 1.96 g of anthraquinone (i.e., 98% of initial amount) with m.p. 278-280° and 1.87 g of 1-anilinoanthraquinone with m.p. 132-134.5°.

Chromatographic isolation of 1-anilino- and 1-N,N-alkylphenylaminoanthraquinones. A sample of 0.4-0.5 g of the mixture of substances obtained by the separation of excess amine (precipitate (II)) was dissolved in 25-30 ml of carbon tetrachloride. The solution was poured into a column filled with anhydrous aluminum oxide. The chromatogram was developed by the same solvent. The mixture separated into a poorly mobile yellow zone and two

more mobile zones (violet and red) which gradually separated from each other. From the separately collected violet-red solution of 1-alkylanilinoanthraquinone and red solution of 1-anilinoanthraquinone the solvent was distilled and the dry residues were weighed. The melting point was determined usually after recrystallization of the residue from alcohol.

1-N,N-Diphenylaminoanthraquinone. A mixture of 1-bromoanthraquinone (5.74 g), diphenylamine (5.1 g), α-chloronaphthalene (30 ml), potassium carbonate (3.28 g) and metallic copper (0.1 g) was stirred for 17 hours at 220°. The precipitate which formed on cooling was filtered off, washed with alcohol and water until neutral, and then dried. There was isolated 1.33 g of light gray product which did not melt at 410° and gave an intense green color with concentrated sulfuric acid and metallic copper, which is characteristic of 1,1-dianthraquinonyl. α-Chloronaphthalene and excess diphenylamine were steam distilled from the filtrate. By fractional recrystallization from ethyl alcohol there was isolated 2.48 g of the product, which gave brown-red prisms which appeared to be purple in transmitted light; m.p. 181-183°.

Found %: C 82.70, 82.74; H 4.61, 4.55; N 3.66, 3.61. $C_{26}H_{17}O_2N$. Calculated %: C 83.20; H 4.53; N 3.73.

SUMMARY

1. The reaction of N-alkylanilines with α-haloanthraquinones was studied. It was established that as the result of the reaction there are formed N-monoaryl substituted derivatives and the products of dehalogenation of 1-haloanthraquinone, in addition to N,N-alkylarylamino substituted anthraquinone.

2. 1-N,N-Methylphenyl-, 1-N,N-ethylphenyl- and 1-N,N-diphenylaminoanthraquinones were synthesized; their properties were described and the light absorption by the solutions of these substances in carbon tetrachloride was measured.

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*Original Russian pagination. See C. B. Translation.

STEROIDS

I. PREPARATION OF 21-BROMOPREGNANOL-17α-TRIONE-3,11,20 FROM PREGNANOL-3β-DIONE-11,20

O. K. Nikiforova and N. N. Suvorov

In the synthesis of cortisone acetate from 11α-hydroxyprogesterone [1] by the methods of Djerassi-Gallaher [2-4] as well as by the method developed in our laboratory [5], the reactive oxo group in 3-position of pregnantrione-3,11,20 is selectively reduced with sodium borohydride with formation of pregnanol-3α-dione-11,20. The resulting substance was subjected to further transformations for the introduction of hydroxy groups in positions 17 and 21. Pregnanediol-3α,17α-dione-11,20 was synthesized through the dienol acetate and the monooxide. By bromination of pregnanediol-3α,17α-dione-11,20 Gallaher and co-workers obtained the corresponding 21-bromo derivative. Hydrolysis of 21-bromopregnanediol-3α,17α-dione-11,20 led to pregnanetriol-3α,17α,21-dione-11,20. Oxidation of the secondary hydroxyl in 3-position gave pregnanediol-17α,21-trione-3,11,20 (dihydrocortisone).

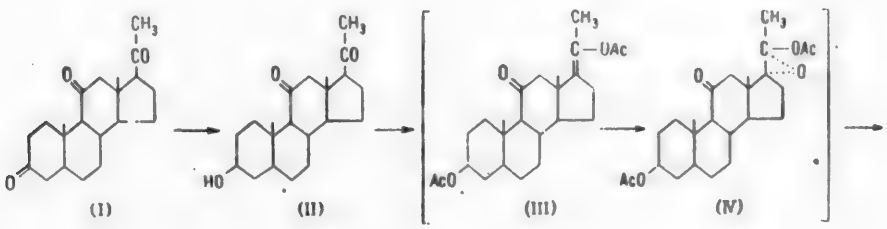
In contrast to the above scheme, in the method from our laboratory, pregnanediol-3α,17α-dione-11,20 was transformed by consecutive or simultaneous bromination and oxidation into 21-bromopregnanol-17α-trione-3,11,20; the replacement of bromine in 21-position by an acetoxy group led to the acetate of dihydrocortisone.

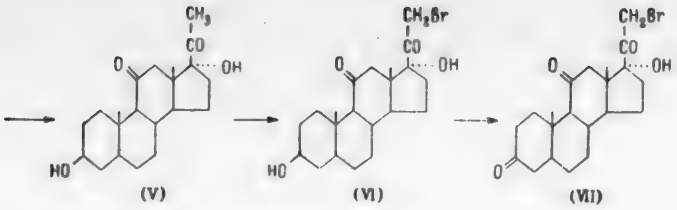
There is an indication in the patent literature [6] that the selective reduction of pregnanetrione over Raney nickel yields not pregnanol-3α-dione-11,20 but its epimer – pregnanol-3β-dione-11,20.

In another patent [7] there is given the most general scheme for transformation of the acetate of pregnanol-3β-dione-11,20 into pregnanediol-3β,17α-dione-11,20 (the constants of this are not cited).

The possibility of construction of a dihydroxyacetone side chain, starting with pregnanol-3β-dione-11,20, is evidently of considerable interest since it opens the possibility to replace the expensive and difficultly obtainable sodium borohydride and to raise the yield of the product considerably in the reduction (96% with nickel instead of 70-72% with sodium borohydride), which facts are very material in the preparation of such an expensive preparation as cortisone, whose synthesis passes through a whole series of steps.

We conducted a synthesis of 21-bromopregnanol-17α-trione-3,11,20 (VII) from pregnanetrione-3,11,20 by the following scheme:





(V) (VI) (VII)

In contrast to the patent data [7], the enolization of (II) was done by us in the medium of acetic anhydride and toluene; we used sulfosalicylic acid for the enolizing reagent [8]. The resulting monoenol acetate (III) was transformed into the oxide (IV) by oxidation with monoperphthalic acid instead of peracetic acid. For hydrolysis of oxide (IV) and preparation of (V) there was used an aqueous methanolic solution of sodium hydroxide. Compounds (III) and (IV) were not isolated in the pure state in the process of this synthesis.

The 21-bromo derivative (VI) was obtained in good yield by bromination of (V) with dioxane dibromide in methanolic medium and the product was smoothly oxidized to (VII) by the action of N-bromosuccinimide.

We consider it a pleasant duty to express our deep gratitude to Iu. N. Sheinker for the spectroscopic studies on the substances prepared by us.

EXPERIMENTAL

Pregnanol-3β-dione-11,20 (II). Into an autoclave made of stainless steel there was placed a solution of 17.2 g of pregnanetrione-3,11,20 (I) in 330 ml of anhydrous methanol and 16.5 g of Raney nickel type W-4. Hydrogenation was run with initial hydrogen pressure of 4 atmospheres for four hours. The reaction product was filtered from the catalyst, the latter was washed on the filter with 30 ml of methanol, the wash liquid was combined with the main filtrate and the methanol was distilled off in vacuo to dryness. To the residue there was added 75 ml of dry ether. A colorless finely crystalline precipitate formed on rubbing. This was filtered off after cooling for two hours in a mixture of ice-salt (−10°); the precipitate was washed with 7 ml of cold ether and dried in vacuum at 40-45°. To the ethereal mother liquor there was added 5 ml of n-heptane. Thereby there was isolated an additional 1 g of the product. After reprecipitation from ether the yield was 0.52 g. The total yield of pregnanol-3β-dione-11,20 was 16.72 g (96.5%); $[\alpha]^{24}D$ + 96° (c 1; $CHCl_3$). The acetate of pregnanol-3β-dione-11,20 has m.p. 163-164°; $[\alpha]^{24}D$ + 98.2° (c 1; $CHCl_3$).

In the infrared spectrum of pregnanol-3β-dione-11,20 in the region of 1350-3500 cm^{-1} there are the following absorption bands: 3403, 2940, 1700, 1456 and 1392 cm^{-1}.

Pregnanediol-3β,17α-dione-11,20 (V). Ten g of pregnanol-3β-dione-11,20 (II) was dissolved in 50 ml of acetic anhydride and refluxed for 40 minutes. The acetic anhydride was distilled completely in vacuum at bath temperature of 60°. The weight of the acetate was 11.2 g. Into a flask, provided with a fractionating column, a distilling condenser and a thermometer, there was placed 20 ml of acetic anhydride, 188 ml of dry toluene and 0.5 g of sulfosalicyclic acid. The apparatus was dried by distilling over two hours some 15 ml of a mixture of acetic acid, acetic anhydride and toluene. Then to the flask contents there was added a solution of 11.2 g of pregnanol-3β-dione-11,20 acetate in 80 ml of a mixture of toluene and acetic anhydride (prepared from 188 ml of toluene and 20 ml of the anhydride) and, over 12 hours, there was slowly distilled 128 ml of a mixture of acetic acid, anhydride and toluene, while 128 ml of a fresh mixture of toluene with acetic anhydride was being added to the reaction mixture at a rate comparable to that of the distillation. The reaction product was cooled to 1°, poured into ice water and stirred for one hour. The aqueous layer was separated from the toluene layer and extracted three times with ether. The toluene and the ethereal layers were combined, washed with 10% solution of sodium bicarbonate and water, until it became neutral, the wash liquid being cooled to 0°. The product was dried with magnesium sulfate. The solvents were removed in vacuum at 40-45° and the monoenol acetate, obtained in the form of a glassy mass, was dried for 4 hours in vacuum at 60°, then for two hours in vacuum over sodium hydroxide at 70-80°. The resulting monoenol acetate (III) was dissolved in 45 ml of dry chloroform, the solution was cooled to −2° and treated with 120 ml of 21% monoperphthalic acid in ether, precooled to −10°. The mixture was allowed to stand for 3 hours at room temperature, after which 115 ml of chloroform was added and the mixture was washed with cooled 2% sodium hydroxide solution until all the precipitated phthalic acid had dissolved.

The chloroform layer was separated, washed with water and dried with magnesium sulfate. The solvent was removed completely in vacuum. The resulting monooxide (IV) was dissolved in 950 ml of methanol and to the solution was added 22 g of sodium hydroxide in 700 ml of water. The reaction mixture was kept one hour at room temperature, neutralized with 1 : 4 hydrochloric acid and extracted with chloroform. The solution of pregnanediol-3β,17α-dione-11,20 in chloroform was washed with water, dried with magnesium sulfate and freed of the solvent in vacuum at 40°. To the residue there was added 40 ml of dry methylene chloride and the mixture was kept for one day at 2°. The resulting precipitate was filtered off, washed with cooled ether and dried in vacuum at 50°. There was obtained 7.68 g of product with m.p. 209-212°. The mother liquor was shaken for 1.5 hours with activated charcoal, the latter was filtered off, washed with 10 ml of methylene chloride, and the solvent was removed from the filtrate until approximately 30% of the original volume remained. The concentrated solution was kept for three days at 2°. In this manner there was obtained additionally 0.53 g of product with m.p. 206-208.5°. After two recrystallizations from benzene there was obtained 6.5 g of pregnanediol-3β, 17α-dione-11,20 (V) (62% calculated on the initial pregnanol-3β-dione-11,20). It formed snow white shiny plates with m.p. 220-222°; $[\alpha]_D^{20}$ +35.13° (c 1; $CHCl_3$).

Found %: C 72.35, 72.42; H 9.05, 8.95. $C_{21}H_{32}O_4$. Calculated %: C 72.41; H 9.19.

In the infrared spectrum of pregnanediol-3β,17α-dione-11,20 in the region of 1350-3500 cm^{-1} there are found the following absorption bands: 3450, 3350, 2940, 1700 and 1456 cm^{-1}.

21-Bromopregnanediol-3β,17α-dione-11,20 (VI). Pregnanediol-3β,17α-dione-11,20 (5.53 g) was dissolved in 170 ml of methanol and to this solution there was added dropwise over 4.5 hours 3.94 g of dioxane dibromide in 15 ml of methanol. After completion of the bromination, the colorless solution was rapidly poured into 2.2 liters of water cooled to 1°. The mixture was stirred for one hour, the resulting white precipitate was filtered off, washed with water and dried in vacuum at room temperature over sulfuric acid. Its weight was 6.44 g; m.p. 216-217°. After two recrystallizations from butyl acetate there was obtained 3.88 g of product with m.p. 227.5-228° (with decomposition). The mother liquor was concentrated in vacuum and 1.6 g of additional product was obtained from it. After recrystallization there was obtained 1.12 g of product with m.p. 227.5-227.7°. The total yield of 21-bromopregnanediol-3β,17α-dione-11,20 was 5 g (73%); $[\alpha]_D^{20}$ + 70.0° (c 1; acetone).

Found %: C 59.73, 59.84; H 7.34, 7.45; Br 18.27, 18.39. $C_{21}H_{31}O_4Br$. Calculated %: C 59.70; H 7.32; Br 18.72.

21-Bromopregnanol-17α-trione-3,11,20 (VII). To 3.8 g of 21-bromopregnanediol-3β,17α-dione-11,20 there was added 130 ml of methanol, 11.5 ml of water and 3.5 g of N-bromosuccinimide. The mixture was stirred in the dark for one day at room temperature. The precipitated crystals were filtered off, washed with cold methanol and dried in a vacuum desiccator over sulfuric acid. Its weight was 2.88 g. The brightly colored methanolic mother liquor was added dropwise to 1% solution of sodium bisulfite cooled to 0°. The resulting colorless precipitate was filtered off, washed with water until neutral and dried over sulfuric acid. After recrystallization from ethylene chloride there was obtained 0.5 g of the product. Both products were combined and recrystallized from ethylene chloride. The yield was 3.02 g (81.6%); m.p. 215-215.5° (with decomposition); $[\alpha]_D^{20}$ +77° (c 1; $CHCl_3$). The mixed melting point of this sample with a sample of 21-bromopregnanol-17α-trione-3,11,20, obtained previously from 21-bromopregnanediol-3α,17α-dione-11,20 showed no depression.

SUMMARY

1. Starting with pregnanol-3β-dione-11,20 there was accomplished the synthesis of 21-bromopregnanol-17α-trione-3,11,20 – an important intermediate in the previously developed scheme for the synthesis of cortisone acetate.

2. A method of hydrogenation was developed for pregnanetrione-3,11,20 to yield pregnanol-3β-dione-11,20 over Raney nickel catalyst of W-4 type at initial hydrogen pressure of 4 atmospheres.

3. Pregnanediol-3β,17α-dione-11,20 and 21-bromopregnanediol-3β,17α-dione-11,20 were prepared and characterized.

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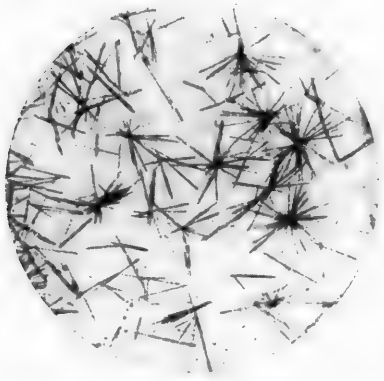
STEROIDAL SAPOGENINS

IV. A NEW SARSAPONINE ISOLATED FROM ROOTS OF YUCCA FILAMENTOSA

O. S. Madaeva

In our previous publication [1] it was shown that from the roots of Yucca filamentosa growing on the Black Sea shores of the Caucasus there was isolated about 0.9% of water insoluble saponines which were gradually precipitated after standing in defatted water solutions – extracts of saponines – the precipitates having the appearance of pinkish-brown fine powder. The present work is a continuation of study of these saponins. The colored precipitate was purified by boiling with ether, recrystallization from acetone with charcoal and several recrystallizations from aqueous butanol; finally there was obtained a colorless crystalline precipitate in the form of long needles collected in bundles (see figure). It melted at 283-284° (with decomposition) and according to its composition corresponded to a glucoside of monohydroxysapogenine, containing two molecules of hexose (saponine I). From this there was prepared an acetate [2], the benzene solution of which was passed for purification through a column with aluminum oxide, weakened preliminarily by washing with ethyl acetate. The acetate in its elemental composition was a completely acetylated form of the above mentioned glucoside. After hydrolysis of the acetate with sodium methoxide [3] there was isolated the original saponine.



Crystals of sarsaponine from Yucca filamentosa (magnified 20 times).

After refluxing saponine I with 4 N aqueous methanolic solution of hydrochloric acid there was obtained, as the result of hydrolysis, 57% of a resinous crystalline precipitate. Double chromatography on paper applied to a sample of this precipitate, in the presence of witness-compounds (sarsapogenine and smylagenine) showed that this precipitate consists only of sarsapogenine. The infrared spectrum of the acetate of the sapogenine turned out to be identical with the infrared spectrum of the acetate of sarsapogenine [4].

For clarification of the composition of the carbohydrate residue of the saponine there was examined the composition of the sugars in the aqueous methanolic solution after the acid hydrolysis of saponine and the extraction of the resulting sapogenine with benzene. We used the technique of ascending paper chromatography. The solvent system was that of a mixture of butanol, pyridine and water (3 : 2 : 1.5) [5]; the chromatogram was developed by spraying with 3% solution of p-anisidine in n-butanol containing 3% of hydrochloric acid [6]. After repeated chromatographing with the witness-compounds there were obtained two spots which corresponded in the values of Rf to glucose and galactose, which fact confirmed the data of the elemental analysis.

From the butanol filtrates after recrystallization of saponine I there was isolated a precipitate with a lower decomposition temperature (274-275°); however, its elemental analysis and the study of the aglucone and sugar residue obtained from it showed that it was identical to sarsaponine I.

Sarsaponines of different compositions have been described by various authors in the literature (see Table).

Comparison of Sarsaponines of Various Compositions

Saponine isolated from	Elemental composition of saponine	M. p.	$[\alpha]_D^{20}$ (in pyridine)	Aglucone	Carbohydrate portion	Lit. ref.
Sarsaparilla Jamaika (roots)	$C_{44}H_{76}O_{20} \cdot 7H_2O$	248°	—48.5°	Sarsapogenine	Dextrose	[7]
Yucca Schotti (fruits)	$C_{27}H_{44}O_3(C_6H_{10}O_5)_3$	241—245		Sarsapogenine		[8]
Yucca Schidigera (leaves)	$C_{45}H_{74}O_{18}$	265—268	—48.3	Sarsapogenine	Glucose, galactose, xylose	[9]
	$C_{57}H_{94}O_{28}$	293—297	—46.8	Sarsapogenine + traces of marcogenine	Five or six molecules of hexose	
Yucca filamentosa (roots)	$C_{27}H_{44}O_3(C_6H_{10}O_5)_2 \cdot H_2O$	283—284	—41.84	Sarsapogenine	Hexose, galactose	Present paper

The sarsaponine isolated by Marker [8] from the fruit of Yucca Schotti and sarsaponines obtained by Wall [9] by enzymic cleavage of natural saponins from the leaves of Yucca Schidigera present the greatest points of interest among these substances; of the latter group, one, as indicated by the author, was contaminated by some marcogenine.

The saponine described by us differs from all those shown in the Table both in composition and in the physical constants; it is a quite individual substance and is a glucoside of sarsapogenine in the composition of which units of glucose and galactose are included.

The infrared spectra were measured by the collaborators of the Physicochemical Laboratory under the direction of Iu. N. Sheinker, for which work I express my gratitude to them.

I express my deep gratitude to L. M. Utkin for the interest shown in this work.

EXPERIMENTAL

Sarsaponine – glucoside of 5β,25α-spirostan-3β-ol. From the defatted aqueous solutions of saponins prepared from the roots of Yucca filamentosa there precipitated, after distilling off methanol and traces of benzene and standing for several days, some fine pinkish-brown precipitate. This was filtered off, washed with water and ether, and recrystallized from acetone (1 : 200) with charcoal, and then twice from aqueous n-butanol (1 : 50); there was obtained a colorless crystalline substance in the yield of 0.9% based on the root weight. It melted with decomposition at 282-284° (saponine I) after having been dried in a vacuum oven at 100° for five hours; $[\alpha]^{20}D$ −41.84° (c 1; pyridine). It crystallizes with a molecule of water and does not liquefy on exposure to air.

Found %: C 61.82, 62.00; H 8.50, 8.71. $C_{27}H_{44}O_3(C_6H_{10}O_5)_2 \cdot H_2O$. Calculated %: C 61.72; H 8.75.

The substance was dried at 100° and 0.1 mm for six hours.

Found %: C 63.33; H 8.71. $C_{27}H_{44}O_3(C_6H_{10}O_5)_2$. Calculated %: C 63.22; H 8.70.

The anhydrous substance gains in weight extremely rapidly by adding a molecule of water.

From the filtrates after the isolation of saponine I there was obtained a precipitate which after recrystallization from methanol had decomposition point at 274-276° (saponine II); this was dried for 4.5 hours at 100° and 15 mm.

Found %: C 61.63; H 8.60. $C_{27}H_{44}O_3(C_6H_{10}O_5)_2 \cdot H_2O$. Calculated %: C 61.72; H 8.75.

Sarsaponine acetate. The saponine (I) (0.3 g) was refluxed for two hours with 1 ml of acetic anhydride in the presence of 1 ml of pyridine. The cooled solution was poured into 10 volumes of water acidified with hydrochloric acid; the resulting somewhat tarry precipitate was extracted with benzene, the benzene solution was washed with water until neutral, dried and shaken with charcoal. After distillation of benzene there remained 0.4 g of a slightly yellowish viscous transparent uncrystallizable mass. For purification this was dissolved in 3 ml of benzene and passed through a column with 1.3 g of aluminum oxide which had been weakened by a preliminary washing with ethyl acetate. Washing with benzene gave 0.34 g of colorless glassy residue which was readily soluble in all organic solvents; on evaporation of such solutions there remained an uncrystallizable film.

Found %: C 61.49, 61.53; H 7.59, 7.68. $C_{53}H_{78}O_{20}$. Calculated %: C 61.48; H 7.59.

Hydrolysis of saponine acetate. The saponine acetate (0.25 g) was dissolved in 3.5 ml of anhydrous methanol and to this was added 7 ml of methanolic solution of sodium methoxide prepared from 0.02 g of sodium. The solution became turbid shortly and after one hour there began to form a colorless crystalline precipitate of the saponine. This was filtered off on the following day, washed with 5 ml of cold alcohol acidified with acetic acid, followed by 2 ml of alcohol and ether. After drying in vacuum at 100° there was obtained 0.15 g of the product with m.p. 282-284°; a small precipitate of the saponine also formed in the filtrate.

Sarsapogenine. The saponine with m.p. 282-284° (0.3 g) was refluxed in a small flask with 28 ml of 50% methanol and 17 ml of concentrated hydrochloric acid in the presence of 10 ml of benzene for four hours. The aqueous methanolic layer was separated, extracted with benzene and left for the determination of sugars. Sapogenine was isolated from the benzene solutions. After recrystallization from ether it did not give a depression in mixed melting point with a specimen of sarsapogenine (m.p.193-196°), while in mixed melting point with a specimen of smylagenine (m.p. 183-184°) melting began at 177°. The isolated sapogenine corresponded to sarsapogenine in the value of its Rf; the infrared spectrum of the acetate prepared from it under conventional conditions gave a complete coincidence with the infrared spectrum of sarsapogenine acetate [9].

Determination of composition of sugars. From the aqueous methanol hydrochloric acid solution the solvents were distilled in vacuum at 45°, methanol being added several times for the complete removal of hydrochloric acid. The determination of sugars in the resulting aqueous solution by means of chromatography on paper gave two spots which in their values of Rf corresponded to galactose and glucose that had been deposited alongside on the paper.

SUMMARY

From the roots of Yucca filamentosa there was isolated one previously undescribed glucoside of sarsapogenine, containing two molecules of hexose in the sugar portion: glucose and galactose.

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STEROIDAL SAPOGENINES

V. SAPOGENINES OF LEAVES OF AGAVE AMERICANA L.

N. A. Serova and O. S. Madaeva

In the study of plants of USSR flora in respect to their content of steroidal saponines there is interest not only in new plant species but also in those in which the steroidal sapogenines had been found previously. The effect of climatic conditions, soil and locality, in which the plant is collected, on the nature of the steroidal sapogenines which enter the composition of the saponines of a given plant, had been noted by a number of authors [1, 2]. This was confirmed by the example of roots of Yucca filamentosa growing on the Black Sea coast of Caucasus and in southwestern parts of Carolina. In the roots of the former there were found sarsapogenine, hytogenine and hecogenine [3, 4] while in the latter there was found hytogenine (about 1.1%) [5].

The present work is devoted to the study of the composition of sapogenines of the leaves of Agave americana L., cultivated on the Black Sea coast of the Caucasus. It is known that Marker [6] had isolated from the leaves of this species a hecogenine (0.4%) which was also obtained by French scientists [7] from the leaves of this Agave grown in the south of France.

We ran the extraction of saponines in a Sohxlet apparatus with a mixture of water and butanol (2 : 3). Xylene was used for defatting of the aqueous solutions of saponines and for further extraction of sapogenines after acid hydrolysis and after the alkaline hydrolysis.

Separation of the summary technical sapogenines was accomplished by the method of chromatography on aluminum oxide; the composition of sapogenines in the eluates was determined by means of paper chromatography [8].

As a result of this work there was obtained hecogenine in 0.2% yield and there was shown the presence of rocogenine on the basis of a comparison of the values of Rf of the substance obtained from methanolic eluates (Rf 0.66) with a sample of rocogenine (Rf 0.62) synthesized by us by reduction of hecogenine with sodium borohydride [9]. The infrared spectra of their acetates proved to be similar.

EXPERIMENTAL

The macerated fibrous mass of dry leaves of Agave (140 g) was extracted in a Sohxlet apparatus with 530 ml of a mixture of butanol and water (3 : 2) over twenty hours. The resulting extract was transferred to a separatory funnel. To the lower aqueous layer (275 ml) there was added 13.75 g of sodium chloride and the solution was adjusted to pH 4-5 with hydrochloric acid. Then the solution was subjected to extraction with saturated aqueous butanol (four times 100 ml each). The wash butanol solutions were added to the main solution and these were washed with 5% solution of sodium chloride at pH 4-5 (1/3 of total volume). To the washed butanol solution of saponines there was added 1/2 volume of water and the butanol was distilled completely in the form of an azeotropic mixture. To the aqueous solution in saponines there was added an equal volume of methyl alcohol, the aqueous alcoholic solution was extracted with xylene (four times) to remove lipoids, after which hydrolysis was run.

The defatted aqueous alcoholic solution of saponines (150 ml), 75 ml of concentrated hydrochloric acid and 150 ml of xylene were refluxed for four hours. After separation in the xylene layer, the aqueous alcoholic layer was subjected to extraction with xylene. The xylene extracts were combined, washed with a saturated solution of sodium chloride and concentrated to the volume of 50 ml. For running the alkaline hydrolysis there

was added 30 ml of 10% methanolic solution of potassium hydroxide and the mixture was boiled for one hour. After cooling, the xylene layer was separated while the aqueous alcoholic layer was extracted several times with xylene. The combined xylene extracts were washed with water until neutral. Xylene was distilled from the xylene solution after having been dried with sodium sulfate and there was obtained 2.4 g of summary sapogenines in the form of a dark crystallizing mass. This mass was dissolved in 35 ml of benzene and deposited on the column with 40 g of activated commercial aluminum oxide. Washing with benzene and a mixture of benzene with chloroform (4:1) led to the separation of oily impurities which do not contain sapogenines; tarry crystalline precipitate passes along with chloroform, this material by its Rf value of 0.72 consisting evidently of hecogenine. The residue in the column was eluted with methanol. From the chloroform eluates containing hecogenine, the solvent was removed by distillation and the residue was washed with heptane, then with cold acetone. After recrystallization from ethyl acetate there was obtained the precipitate with m.p. 244-247°. This substance by its elemental composition, specific rotation and m.p. corresponded to hecogenine [3, 4, 6].

2,4-Dinitrophenylhydrazone of hecogenine was obtained by mixing hot saturated alcoholic solutions of hecogenine and 2,4-dinitrophenylhydrazine (1:1) in the presence of hydrochloric acid. The 2,4-dinitrophenylhydrazone of hecogenine formed thin yellow needles from ethyl alcohol; m.p. 244-246° (with decomposition).

Found %: N 9.07. $C_{33}H_{46}O_7N_4$. Calculated %: N 9.2.

Hecogenine acetate was prepared by refluxing hecogenine with three parts of acetic anhydride for thirty minutes. The product was recrystallized from acetone. M.p. 241-243°.

Literature data: 243°, 252° [6]. Its infrared spectrum agreed completely with those described in the literature [10].

The residues of methanolic eluates were an uncrystallizable tarry mass. By means of paper chromatography there were obtained two spots with Rf values of 0.62 and 0.76 (solvent – mixture of iso-octane, chloroform and acetic acid: 100:40:4). After treatment with Girard T reagent [11] hecogenine was isolated from the ketonic fraction. The resulting spot from a sample taken from the nonketonic fraction had the Rf value of 0.66 (solvent – mixture of iso-octane, chloroform and acetic acid: 100:40:4). After deposition on paper, the synthetic hecogenine had Rf 0.62.

Acetylation of samples of the nonketonic fraction and of the prepared sample of rocogenine (for infrared spectra) was run under the usual conditions by refluxing with acetic anhydride for 3-4 minutes.

SUMMARY

1. It was shown that leaves of Agave americana L. cultivated on the Black Sea coast of the Caucasus contain 0.2% of hecogenine with a small admixture of rocogenine.

2. For isolation of sapogenines there was used the method of extraction with aqueous butanol and by defatting with xylene.

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EFFECT OF SUBSTITUENTS IN THE MOLECULES OF INHIBITORS ON THEIR PROTECTIVE PROPERTIES IN AUTOXIDATION OF α-PINENE

E. N. Novikova

The purpose of this work is the study of the process of autoxidation of α-pinene in the presence of an initiator and antioxidants in connection with the various chemical nature and structure of their molecules.

It is known that α-pinene, as an unsaturated compound, is readily subjected to autoxidation [1], which is accelerated by oxides and salts of metals [2]. The facile oxidizability of α-pinene is also connected with the fact that phenols contained in turpentine are extracted from the latter in the process of purification and fractional distillation and thus α-pinene is deprived of the natural antioxidants. Therefore for the retardation of autoxidation of α-pinene it is necessary to add antioxidants to it.

One might expect that stabilization of α-pinene by inhibitors, just as in the case of cracked gasolines [3], is more advantageous economically than is its purification by a second distillation. The primary products of autoxidation of α-pinene are hydroperoxides [4, 5] which initiate the process of its further oxidation. Termination of this chain reaction of autoxidation may be realized by reaction of antioxidants with the radical of the hydrocarbon undergoing the oxidation or with oxygen [6].

The inhibiting action of antioxidants depends on the chemical nature and structure of their molecules [7, 8]. Therefore for comparative evaluation of the activity of inhibitors and for the approach to the explanation of the mechanism of their action, it was interesting to follow the accumulation of peroxide compounds in α-pinene.

EXPERIMENTAL

α-Pinene that was used was taken from production, being obtained from dry distillation turpentine; it was twice distilled from metallic sodium; b.p. 155° at 760 mm, d^{20}_4 0.8576, $n^{20}D$ 1.4657.

For retardation of the process of autoxidation of α-pinene, there were added to it: phenols, phenol derivatives, diphenylamine, naphthalene and other compounds, in amounts of 0.01 millimole of antioxidant per one mole of α-pinene. The autoxidation of α-pinene proceeded in air in diffuse daylight. α-Pinene, both pure and that with added antioxidants, was poured in 24 ml lots into wide-necked flasks of 100 ml capacity, which were left open at 18-20° for prolonged periods.

After definite time intervals samples were taken and in these there were determined, by iodometric method [9], the amounts of peroxide compounds that were present. To a sample of the self-oxidizing α-pinene (about 1 g) there was added 15 ml of 98% acetic acid and 5 ml of 20% potassium iodide solution. The mixture was allowed to stand for 15 minutes at 20°, then the separated iodine was titrated with 0.1 N solution of sodium thiosulfate. A blank run was made in parallel. The amount of peroxide compounds was calculated in milliliters of 0.1 N solution of sodium thiosulfate per 100 g of α-pinene.

For titration of 1.0162 g of α-pinene after 30 days of autoxidation there was required 7.95 ml of 0.1 N sodium thiosulfate. For titration of 0.9846 g of α-pinene after 30 days of autoxidation in the presence of hydroquinone there was required 1.6 ml of 0.1 N sodium thiosulfate. In the blank experiment there was consumed 0.1 ml of 0.1 N sodium thiosulfate. Thus, the amount of peroxide compounds in 100 g of the oxidized α-pinene was equal to 772.5 ml of 0.1 N sodium thiosulfate, while per 100 g of α-pinene oxidized with addition of hydroquinone this amount was equal to 152.5 ml of 0.1 N sodium thiosulfate. For titration of 0.0896 g of freshly

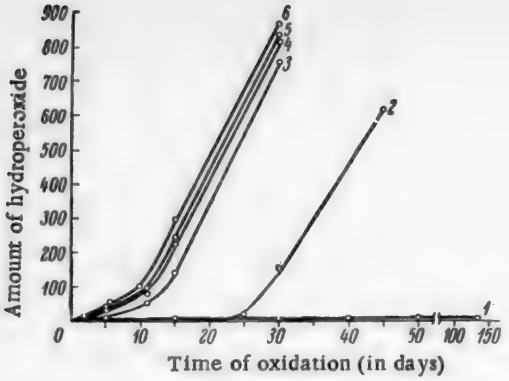

Fig. 1. Effect of phenols and their derivatives on formation of peroxide compounds in α-pinene. 1) Pyrocatechol, pyrogallol, o-aminophenol and p-aminophenol; 2) hydroquinone, 3) thymol, 4) guaiacol and orcin, 5) p-butylphenol and p-cumylphenol, 6) α-pinene without additives.

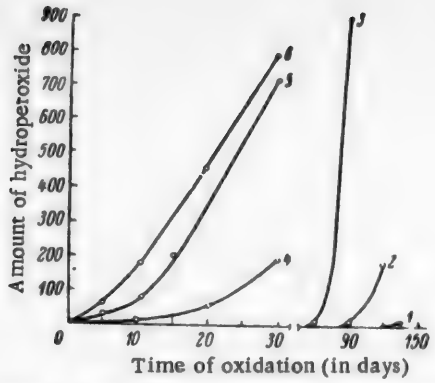

Fig. 2. Effect of derivatives of biphenyl and other compounds on formation of peroxide compounds in α-pinene. 1) p-Aminodiphenylamine, 2,4-diaminodiphenylamine, p-hydroxydiphenylamine and 1,4-diphenylphenylenediamine; 2) diphenylcarbazide; 3) diphenylcarbazone; 4) diphenylamine; 5) phenylsemicarbazide; 6) α-pinene without additives.

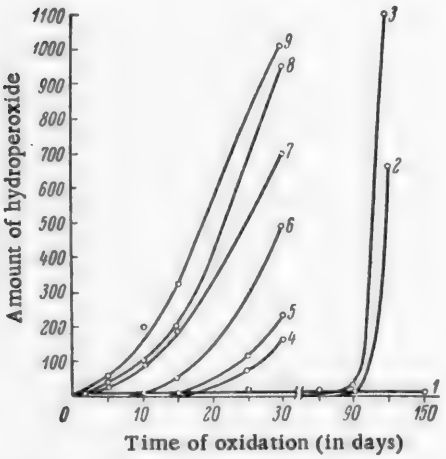

Fig. 3. Effect of derivatives of naphthalene on formation of peroxide compounds in α-pinene. 1) Dinaphthylphenylenediamine; 2) α-naphthol; 3) p-hydroxyneozone D; 4) α-naphtholphthalein; 5) β-naphthol; 6) neozone D; 7) α-naphthylamine; 8) naphthol AS; 9) α-pinene without addends.

distilled α-pinene there was required 0.1 ml of 0.1 N sodium thiosulfate, i.e., peroxide compounds were absent.

Along with the determination of peroxide compounds, the autoxidation of α-pinene was followed by determinations of its index of refraction (with Abbe refractometer) and density. These measurements showed that in α-pinene in the absence of antioxidants (such as pyrocatechol or p-hydroxy diphenylamine) during the induction period of oxidation (Fig. 1-3) the peroxide compounds were not formed in measurable (by titration) amounts. Here the density (d^{20}_4 0.8579) and index of refraction ($n^{20}D$ 1.4659) remained almost the same as in the original α-pinene. Conversely, pure α-pinene, after three months of autoxidation, was characterized by the following constants: d^{20}_4 0.9660, $n^{20}D$ 1.4832, i.e., α-pinene untreated with an antioxidant suffers a deep-seated oxidation.

Experimental data (Fig. 1-6)* show that the various (in their chemical nature) antioxidants inhibit the process of formation of peroxides in α-pinene to different degrees. Phenols (Fig. 1) with hydroxy groups in ortho-position (pyrocatechol and pyrogallol), o- and p-aminophenols, are active inhibitors of the process of formation of peroxide compounds in α-pinene, while the m-isomers (resorcinol and m-aminophenol) do not show the inhibiting action. Replacement of hydrogen in one of the hydroxy groups in the pyrocatechol molecule by a methyl group (guaiacol) sharply lowered the high inhibitory activity of pyrocatechol. The complication of the hydroquinone molecule by replacement of its polar group HO by the group $C(CH_3)_3$ (p-butylphenyl) or by the group $C_6H_5C(CH_3)_2$ (p-cumylphenol) caused a weakening of the antioxidant action.

*In all graphs the amount of hydroperoxide is expressed in milliliters of 0.1 N solution of sodium thiosulfate per 100 g of α-pinene.

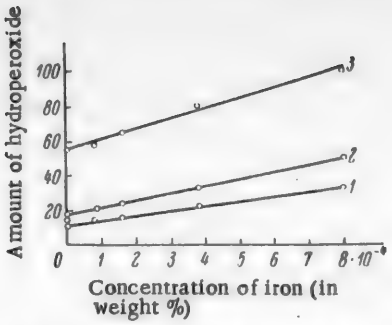

Fig. 4. Effect of iron palmitate on formation of peroxide compounds in α-pinene.
1) After 2 days, 2) after 3 days, 3) after 9 days of autoxidation.

Diphenylamine (Fig. 2) weakly inhibits the formation of peroxides in α-pinene. Introduction of the NH_2 group (p-aminodiphenylamine) or the NHC_6H_5 group (1,4-diphenylphenylenediamine) into the molecule of diphenylamine leads to a sharp increase of the inhibiting action. In comparing the inhibiting activity and the structural formulas of diphenylcarbazide and diphenylcarbazone one may suppose that the high activity of the former is connected with the presence of four secondary amine groups in its molecule. The relatively smaller activity of diphenylcarbazone is evidently connected with the replacement of two amino groups by an azo group.

In examining the retarding action of naphthalene derivatives (Fig. 3; β-naphthol, β-naphthylamine naphthol AS) it is clear that the nature and the polarity of the substituent groups HO, NH_2 and $CONHC_6H_5$ exert their effect on

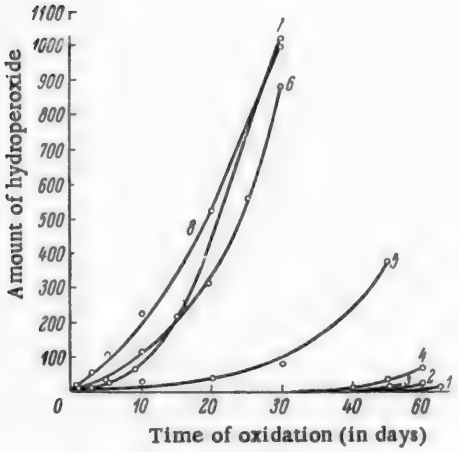

Fig. 5. Effect of antioxidants on formation of peroxide compounds in α-pinene containing iron palmitate.
1) p-Hydroxydiphenylamine, 2) o- and p-aminophenols, 3) 2,4-diaminodiphenylamine, 4) p-aminodiphenylamine, 5) diphenylamine, 6) α-pinene without addends, 7) pyrocatechol, 8) α-pinene with iron palmitate.

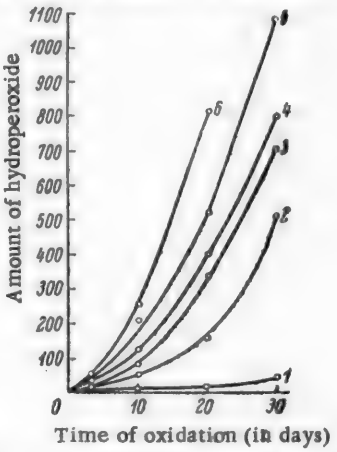

Fig. 6. Effect of derivatives of naphthalene on formation of peroxide compounds in α-pinene containing iron palmitate.
1) p-Hydroxyneozone D, 2) neozone D, 3) β-naphthol, 4) α-pinene without additives, 5) β-naphthylamine, 6) α-pinene with iron palmitate.

the activity of the inhibitor in the formation of peroxides in α-pinene. The ability of the molecule to donate its mobile hydrogen [10] and thus to retard to a greater or lesser degree the process of autoxidation, and hence the process of formation of peroxides, it is connected with polarity.

In α-pinene during contact with metallic parts of equipment (in the process of its production from turpentine), pipes and tanks, there accumulate compounds of iron which may accelerate autoxidation of α-pinene and our experiments showed (Fig. 4) that an insignificant amount of iron (0.794×10^{-4}%) introduced into α-pinene in the form of iron palmitate accelerated the accumulation of peroxides in α-pinene. As to the activity of inhibitors in the presence of iron palmitate (1 mg of iron per 100 ml of α-pinene), the data obtained by us (Figs. 5 and 6) show that the effective inhibitors of accumulation of peroxides in α-pinene are the compounds which contain simultaneously both amino and hydroxy groups: p-hydroxydiphenylamine, o- and p-aminophenols and p-hydroxyphenyl-β-naphthylamine.

SUMMARY

1. The relative activity of inhibitors on the process of formation of peroxide compounds in α-pinene in diffuse light at 18-20° was studied.

2. It was established that the formation of peroxides in α-pinene is retarded by addition (0.001%) of pyrocatechol, pyrogallol, p- and o-aminophenols, p-hydroxydiphenylamine, dinaphthylphenylenediamine, 1,4-diphenylphenylenediamine, p-aminodiphenylamine, α-naphthol and p-hydroxyphenyl-β-naphthylamine.

3. It was found that derivatives of phenols: guaiacol, orcin, thymol, p-butylphenol and p-cumylphenol (0.01 millimole per 1 mole of α-pinene) are weak inhibitors of accumulation of peroxides in α-pinene.

4. It was shown that the initiating action of iron palmitate on the formation of peroxides exists and the relative activity of o- and p-aminophenols, derivatives of diphenylamine and naphthalene in the presence of iron palmitate was studied.

5. It was shown that the activity of the inhibitor is determined by two factors – polarity of the inhibitor molecule and the mobility of hydrogen connected with the polarity.

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LETTERS TO THE EDITOR

ABOUT PROPERTIES OF POLYAMIDES WITH SILOXANE GROUPINGS

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The considerable interest aroused by organosilicon compounds led us to take up a study of the problem of whether or not siloxane groups in the chain of a dicarboxylic acid affect the properties of polyamides incorporating such an acid. For this purpose we prepared polyamides from three dicarboxylic acids of the following structures:

$$\text{HOOC}-(\text{CH}_2)_2-\text{Si}(\text{R}_1\text{R}_2)-\text{O}-\text{Si}(\text{R}_1\text{R}_2)-(\text{CH}_2)_2-\text{COOH},$$

where 1) $R_1 = R_2 = CH_3$, 2) $R_1 = R_2 = C_2H_5$, 3) $R_1 = CH_3$, $R_2 = C_2H_5$.

From these acids there was prepared a series of polyamides by polycondensation with various aliphatic and aromatic diamines. In addition, from mixtures of these acids and from mixtures of these acids with adipic acid with hexamethylenediamine there were prepared several series of mixed polyamides.

The study of these polyamides showed that the introduction of the siloxane links leads to the formation of polymers having rubber-like properties as well as lower melting points in comparison with polymers from azelaic acid. This is evidently dependent both on the effect of the siloxane grouping and on the presence of side chain substituents present at the silicon atom. In favor of this explanation there is the circumstance that replacement of the methyl radicals of the silicon atom by ethyl radicals causes a lowering of the melting point. The presence of side substituents is the cause for the hindrance of packing of the chains and of their orderliness. Therefore it is not surprising that after prolonged standing the polyamides prepared by us slowly crystallized, which fact is reflected in the rise of melting point and formation of turbidity, as well as decrease of elasticity.

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THE PROBLEM OF THERMODYNAMIC STUDY OF LOWER CHLORIDES OF WOLFRAM (TUNGSTEN)

S. A. Shchukarev, G. I. Novikov and N. V. Andreeva

The density of saturated and unsaturated vapor of wolfram pentachloride was measured by the static method with a quartz membrane null manometer. It was shown by the optico-tensimetric method that gaseous wolfram pentachloride disproportionates forming in the gaseous phase wolfram tetra- and hexachlorides. Direct measurement of molecular weight of the vapor of wolfram pentachloride established the presence in it of up to 10% of dimer W_2Cl_{10}.

The densities of disproportionation of wolfram tetra- and di-chlorides were also measured by the static method with a quartz membrane. The results of the measurements showed that the tetrachloride disproportionates with formation, in the gas phase, of wolfram pentachloride, while WCl_2 disproportionates with formation of penta- and tetrachlorides of wolfram. From the data on measurement of vapor densities we calculated the thermodynamic characteristics of the process (see table).

Processes	ΔH (in kilo-calories)	ΔS (in entropy units)	Temperature interval
$[WCl_5]_{sol} = (WCl_5)_{vap}$	18.5 ± 0.5	33.1 ± 0.7	150 — 253° (M. p. 253°)
$(WCl_5)_{liq} = (WCl_5)_{vap}$	13.6 ± 0.9	23.9 ± 0.9	253 — 330° (B. p. 288°)
$(W_2Cl_{10})_{vap} = 2(WCl_5)_{vap}$	7.9 ± 0.7	13.9 ± 0.9	280 — 450
$2(WCl_5)_{vap} = (WCl_4)_{vap} + (WCl_6)_{vap}$	~ 6	~ -5	300 — 500
$3[WCl_4]_{sol} = [WCl_2]_{sol} + 2(WCl_5)_{vap}$	66 ± 4	90 ± 4	300 — 430
$[WCl_2]_{sol} + 2(WCl_5)_{vap} = 3(WCl_4)_{vap}$	50 ± 4	60 ± 4	450 — 600
$2[WCl_2]_{sol} = [W]_{sol} + (WCl_4)_{vap}$	59 ± 2	67 ± 2	490 — 580
$5[WCl_2]_{sol} = 3[W]_{sol} + 2(WCl_5)_{vap}$	129 ± 4	145 ± 4	490 — 580

Insofar as the experimentally secured thermodynamic characteristics of the processes carried out above are absent from the literature, while Brewer's data published in this monograph have primarily a calculational character, we may consider that the values obtained by us are evidently more accurate than those accepted in various tables.

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CONCERNING THE ORDER OF ADDITION OF WATER AND ALCOHOLS TO VINYLALKYLACETYLENES

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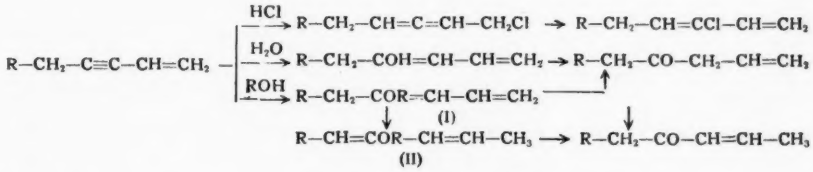
We discovered during a study of reactions of addition to vinylalkylacetylenes that the order of addition of water, alcohols and hydrogen halides to these compounds is not the same. In case of water and alcohols, the hydrogen adds to the second atom of the conjugated system, while in case of hydrogen halides the hydrogen adds to the first atom. Thus in these reactions the atoms of the conjugated system change their polarity.



The order of addition of hydrogen halides to vinylalkylacetylenes has been established previously [1, 2].

The structure of ketones formed in hydration of vinylmethyl- and vinylethylacetylenes in the presence of mercuric sulfate was proved by hydrogenation to the corresponding saturated ketones (methyl propyl ketone and ethyl propyl ketone) and by their infrared spectra. The products contained a small admixture of allyl ketones.

The structure of ethers formed as the result of addition of alcohols to vinylmethyl- and vinylethylacetylenes in the presence of potassium hydroxide at 150° was established by their infrared spectra (only the frequencies of 1,3-diene group are present) and by their transformation under the action of dilute sulfuric acid into the corresponding alkyl propenyl ketones, which were then reduced over palladium on calcium carbonate to methyl and ethyl propyl ketones.

The spectral data indicate that along with ethers (I) there are also formed the products of their isomerization – ethers (II).

The nonconcordance of the order of addition of water and alcohols to that of hydrogen halides may be explained, in our opinion, by the differences in the mechanism of addition of these substances and by the ease of redistribution of electron density in molecules of vinylalkylacetylenes (dipole moment of vinylalkylacetylenes is low in comparison with that of vinylacetylene and is equal to about 0.6 D). Both electrophilic addition of a proton and the nucleophilic addition of the OR anion or some complex with participation of water in the Kucherov reaction, begin at the first carbon atom, since only this order of addition leads to the origin of a stable cation or anion with preservation of conjugation. This explanation meets a difficulty in connection with the fact that isoalkenylacetylenes (for example, isopropenylacetylene) also have lowered values of dipole moments but add hydrogen halides, water and alcohols in the same order (this was studied by many authors).

The discovered regularity should have a general explanation, one common for the reactions of addition of water and alcohol to divinylacetylenic hydrocarbons discovered by I. N. Nazarov [3]. We believe that the solution of this problem is of general interest for the theory of reactions of conjugated systems.

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